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FINAL REPORT

BIOMEDICAL ENGINEERING SUPPORT

Contract EY-76-S-02-2155.000-21

MASTER

Principal Investigator:

W. J. Kolff, M.D., Ph.D.

Co-Investigators and Prepared by:

G. Sandquist, Ph.D.

D. B. Olsen, D.V.M.

L. M. Smith, Ph.D.

Final Report for

June 15, 1971 to June 30, 1979

Institute for Biomedical Engineering and

Division of Artificial Organs

Building 518

University of Utah

Salt Lake City, Utah 84112

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ABSTRACT

On June 15, 1971 the Institute for Biomedical Engineering at the University of Utah contracted with the U.S.A.E.C. to provide biomedical support for an Artificial Heart Program. The goal of the Program was to conceive, design, construct and test a prototype artificial heart system powered by an implantable radio isotope heat source. The system would serve as a total artificial heart for animal experiments and for studies directed at developing a total heart replacement system for humans.

The major responsibilities of the Institute during the eight year contract period were to design, construct and test all blood handling components of the system and prove in vivo accommodation, performance and adequacy of the system in experimental animals.

Upon completion of development of the Implantable Version of the Bench Model Blood Pump, a long series of comprehensive in vitro and in vivo experiments were conducted. In vivo experiments with the system conducted in calves demonstrated the general accommodation, adequate performance and good capacity to sustain the calf as a heart model for up to 36 days. During the more successful in vivo experiments the implanted calves were able to eat, drink, stand, exercise on a treadmill, and exhibited normal blood chemistry and pulmonary function.

LIST OF FIGURES AND TABLES:

I. SUMMARY

On June 15, 1971 the Institute for Biomedical Engineering at the University of Utah contracted with the U.S. A.E.C. to provide biomedical support for the A.E.C.'s Artificial Heart Program. The programmatic goal of the Artificial Heart Program was to conceive, design, construct and test a prototype artificial heart system powered by an implantable radio isotope heat source. The prototype system would be capable of serving as a total artificial heart for animal experiments and for studies directed at developing a satisfactory total heart replacement system for humans.

The major contractual responsibilities of the Institute during the eight year contract period were to design, construct and test all blood handling components of the system and prove in vivo accommodation, performance and adequacy of the system in experimental animals. The blood handling parts had to interface and perform satisfactorily with the mechanical actuator and the thermal converter. The complete system had to perform as an integrated, self contained, totally implantable system.

A reference study made early in the program was a determination and evaluation of the mean performance variables and parameters of the natural heart in an adult male and female. These data provided a performance criteria for the artificial heart system to be developed.

An initial design of a biventricular blood pump, the Bench Model Pump, was then conceived by the Institute. The pump proved to be compatible with the power supply, i.e. the thermal converter (a one cylinder Stirling Cycle engine driven by a Pu-238 heat source) under development by Westinghouse and North American Philips. In concert with the pump development the Institute then selected, fabricated and tested the blood contacting materials on the bench model pump.

A series of abdominal implants of inert models of the thermal converter were conducted by the Institute and biocompatibility, fit and acceptable accommodation was demonstrated in the calf as an animal model for the artificial heart system.

Early in vivo experience with the Bench Model Blood Pump and an externally located electric motor driver for the pump generated preliminary surgical protocols and provided initial accommodation and performance evaluation of the system. It was realized that a method for rapid and individual attachment of the giant vessels and atria to the pump was essential and a system of "quick connects" was developed. These connectors have evolved and improved during the contract to the point where these quick connects are used in all artificial heart systems now under study by the Institute.

Some early in vivo experiments with the Bench Model Blood Pump were terminated by abrupt failure of the flexible shaft which transmitted rotory power from the electric motor driver to the blood pump. After the 7th in vivo experiment all subsequent experiments had the electric motor driver located in the abdomen or the thorax.

In anticipation of receiving the thermal converter with a Pu-238 heat source, an application was prepared and filed by the Institute with the A.E.C. for a Special Nuclear Materials License to receive, store, utilize and ship Pu-238 in conjunction with the Artificial Heart Program. The license was granted to the Institute, but Pu-238 heat sources were not transferred to the Institute due to termination of the program.

Upon completion of the Implantable Version of the Bench Model (called I.V.B.M.) Blood Pump, a long series of comprehensive in vitro and in vivo experiments were conducted.

The Institute designed, constructed and tested the blood handling components for the I.V.B.M. system. An exhaustive series of in vitro testing showed a slight imbalance in the output of the right ventricle over the left ventricle under physiological conditions so a modification to both the ventricle housing (change in compliance) and the displacement volume was implemented. Also, in vitro tests established the blood damage associated with the I.V.B.M. Pump and this damage, related to an hemolysis index, was found to be acceptable and low compared to other pumps then in use in artificial heart research.

In vivo experiments with the I.V.B.M. system conducted in calves demonstrated the general accommodation, adequate performance and good capacity to sustain the calf as a heart model for up to 36 days with this system. During the more successful in vivo experiments the implanted calves were able to eat, drink, stand, exercise on a treadmill, and exhibited normal blood chemistry and pulmonary function.

Near the conclusion of the contract, when it was recognized that an operational thermal converter would not be available, design modification was made to the pump to allow direct attachment of a small integral electric motor which attached directly to the pump and provided a self-contained electric driver and blood pump. Only a few in vivo experiments with the integral I.V.B.M. Blood Pump were conducted before the contract terminated but average survival times of 12 days were realized with this promising system.

II. INTRODUCTION

A programmatic goal was established by the U.S. Atomic Energy Commission in 1971 to develop, design and construct a prototype artificial heart system which would employ an implantable radioisotope power source and would be capable of serving as a total artificial heart system for animal experiments and studies directed at developing and evaluating a satisfactory total heart replacement system for humans.

The AEC Artificial Heart Program employed a coordinated program of continued iterative research and development and in vivo and in vitro experimental testing and evaluation. An implantable version of the bench model (IVBM) system was developed under the Program and provided to the Institute for Biomedical Engineering for extensive in vivo evaluation in calves. It was assumed that a prototype Mark I system would then be developed and undergo extensive design, construction testing and evaluation phase directed at the eventual design, development and construction of a clinical prototype system.

The major responsibility of the Institute for Biomedical Engineering at the University of Utah, under the DOE Artificial Heart Program, was to prove accommodation, performance and adequacy of the artificial heart system and its components as they were developed in the DOE Program and provided to the Institute for study. The Institute also had the responsibility of designing, constructing and testing the blood handling components of the blood pump and ensuring reliability, durability and satisfactory performance of those system components.

Perhaps the best introduction and general description of the DOE Artificial Heart Program as conceived is that written by Jack Kolff, M.D. (who was an investigator under the Contract), a practicing cardiovascular surgeon for the medical journal "Resident and Staff Physician" in December 1976. The journal article follows.

journal articles removed (pages 4 - 8)

III. PROGRESSIVE ACCOMPLISHMENTS DURING CONTRACT TENURE

During the tenure of the eight year Biomedical Engineering Support Contract (June 15, 1971 to June 30, 1979) between the Institute for Biomedical Engineering and the U.S. Department of Energy (initially the U.S. AEC, then ERDA and now DOE), the Institute made progressive accomplishments which were reported to DOE in twenty quarterly and annual progress reports. These accomplishments are epitomized within each contract year to provide a chronological account of progress under the program.

Period from June 1971 through August 1972

1. A daily power profile for an artificial heart has been established from the literature.
2. The power input and output of the K_{wan}-Gett Artificial Heart has been determined in vitro. Overall performance of this pneumatic system has been established.
3. In vitro performance of the Kwan-Gett heart has been verified in vivo.
4. In vitro testing protocol has been established and significant experiments established.
5. A preliminary design of a mechanically driven total artificial heart has been made which is suitable for the AEC Total Artificial Heart system.

Period from August 1972 through August 1973

1. Established by animal trial fit experiments, optimum location and configuration of the blood pump connectors and housing.
2. Designed, selected and tested materials and constructed the passive blood handling parts of the bench model blood pump.
3. Implanted inert dummy models of the thermal converter in eight calves to determine surgical procedures, optimum location and fit, animal tolerance and chronic effects. Results showed that the thermal converter can be accommodated in the abdomen of calves.
4. Constructed and instrumented a mock circulation system for in vitro testing of the blood pump.
5. Performed extensive testing and characterization of the bench model blood pump.
6. Designed, constructed and currently testing a quick connect system for rapid anastomosis of the atrial cuffs and arterial grafts to the blood pump.
7. Established a preliminary protocol for animal implantation of the bench model blood pump.

Period from August 1973 through August 1974

1. Designed, constructed and tested the blood handling components for the bench model blood pump in collaboration with Westinghouse Astronuclear Laboratory. These components included the ventricle diaphragms and domes, valves, and blood vessel connectors with quick connects.

2. Performed a series of nine total heart replacement intrathoracic experiments in calves with the bench model blood pump and both externally and internally located electric motor drives to provide pumping power. These experiments demonstrated preliminary practicability of the implantation assessment.

3. Determined the in vivo performance of the Bench Model System in calves.

4. Prepared and filed an application to the Division of Material Licensing of the AEC for a Special Materials License to receive, store, utilize and ship radioactive materials used in conjunction with the AEC Artificial Heart Program.

5. Facilities and procedures for receiving, storing, handling, testing and shipping those radioactive materials in collaboration with Westinghouse Astronuclear Laboratories were developed. Tentative procedures and a protocol for the implantation in experimental animals of systems or subsystems of the AEC Artificial Heart, which contain radioactive materials have been established.

Period from August 1974 through August 1975

1. Designed, constructed and began testing of the blood handling components for the Implantable Version Bench Model (IVBM) Blood Pump in collaboration with the Westinghouse Astronuclear Laboratory. The blood handling components are the ventricle, diaphragms and domes, the valves and blood vessel connectors. In vivo tests with the Bench Model and IVBM Blood Pump supplied by ERDA were conducted to determine pump performance, efficiency, durability and reliability of both the blood handling components and the Blood Pump drive mechanism.

   Information and recommendations obtained under these task assignments were provided to ERDA and others as directed for development of the Intermediate and Prototype Systems.

2. Engaged in vitro and in vivo studies to determine and evaluate the pumping performance and long-term reliability and mechanical behavior of the Bench Model Blood Pump ventricles some of which were prepared with selected grafting substrate surfaces in cooperation with Dr. Joseph Andrade (Co-Director of U.S. ERDA Contract E(11-1)-2147 at the University of Utah) and others.

3. Performed a series of total heart replacement (in vivo) experiments in animals using the Bench Model Blood Pump to replace the animal's natural heart. This Blood Pump was powered by an electric motor located abdominally in the animal.

In vivo experimental data concerning cardiac output, systemic blood pressures, efficiencies, physiological and anatomical accommodation, heating levels and general performance of the Implantable System have been provided as required under the contract.

4. Developed and began the evaluation of complete procedures and methods for the receipt, storage, preparation, implantation, monitoring, testing, removal and shipment of the IVBM Artificial Heart System. These procedures and methods have been established for the IVBM System employing either an implantable electric motor power supply and/or the IVBM Thermal Converter System with a Pu-238 heat source.

5. Provided to ERDA and other organizations as designated, information, data, observations and recommendations and general expertise and competence for the development evaluation of programs and systems under the Artificial Heart Program.

6. Updated the base concerning the power requirements for the Artificial Heart System and provided practicability investigation and recommendations on the incorporation of control systems utilizing important physiological parameters into the design and construction of the Intermediate Artificial Heart System.

7. Investigated techniques for determining cardiac output and other pumping performance parameters of the in vivo system using a NASA developed implantable data telemetry system.

Period from August 1975 through August 1976

1. Designed, constructed and began testing of the blood handling components for the Implantable Version Bench Model (IVBM) Blood Pump in collaboration with the Westinghouse Astronuclear Laboratory. The blood handling components are the ventricle, diaphragms and domes and the valves and blood vessel connectors. In vivo tests with the Bench Model and IVBM Blood Pump supplied by ERDA were conducted to determine pump performance, efficiency, durability and reliability of both the blood handling components and the Blood Pump mechanism.

   Information and recommendations obtained under this task assignment were provided to ERDA and others as directed for development of the Mark I System.

2. Engaged in vitro and in vivo studies to determine and evaluate the pumping performance and long-term reliability and mechanical behavior of the IVBM Blood Pump.

3. Performed a series of total heart replacement (in vivo) experiments in animals using the Bench Model and IVBM Blood Pump to replace the animal's natural heart. The Blood Pumps are powered by an electric motor located abdominally in the animal.

In vivo experimental data concerning cardiac output, systemic blood pressures, efficiencies, physiological and anatomical accommodation, heating levels and general performance of the Implantable System have been provided as required under the contract.

4. Developed and began the evaluation of complete procedures and methods for the receipt, storage, preparation, implantation, monitoring, testing, removal and shipment of the IVBM Artificial Heart System. These procedures and methods have been established for the IVBM System employing either an implantable electric motor power supply and/or the IVBM Thermal Converter System with a Pu-238 heat source.

5. Provided to ERDA and other organizations as designated, information, data, observations and recommendations and general expertise and competence for the development evaluation of programs and systems under the Artificial Heart Program.

6. Determined and evaluated performance of the Bench Model and began performance studies with the IVBM System in experimental animals during rest, standing and exercise.

Period from August 1976 through June 1979

1. Designed, constructed and tested the blood handling components for the implantable version bench model (IVBM) blood pump in collaboration with the Westinghouse Astronuclear Laboratory. The pusher cup of the right ventricle was made smaller to correct a pumping imbalance between the left side (which pumps against higher pressure) and the right side. The pump with this modification was called the "ΔV" pump. The blood handling components are the ventricle, diaphragms and domes, and the valves and blood vessel connectors. In vivo tests with the blood pumps supplied by ERDA were conducted to determine pump performance, efficiency, durability and reliability of both the blood handling components and the blood pump drive mechanism.

2. Engaged in vitro and in vivo studies to determine and evaluate the pumping performance and long-term reliability and mechanical behavior of the ERDA Blood Pump.

3. Performed a series of total heart replacement experiments (in vivo) in animals using the ERDA Blood Pump, to replace the animal's natural heart. The blood pumps were powered by an electric motor located in the abdominal wall of the animal.

   In vivo experimental data concerning cardiac output, systemic blood pressures, efficiencies, physiological and anatomical accommodation, heating levels and general performance of the ERDA system were provided as required under the contract. Specifically, the pumping imbalance noted under Item 1 was corrected after a ΔV pump was developed.

4. Developed complete procedures and methods for the receipt, storage, preparation, implantation, monitoring, testing, removal and shipment of the artificial heart system. These procedures and methods have been established for the IVBM system employing either an implantable electric motor power supply and/or the IVBM thermal converter system with a Pu-238 heat source. It was not known at the time that the Pu-238 heat sources would not be delivered as planned.

5. Provided to ERDA and other organizations as designated, information data, observations and recommendations and general expertise and competence for the development evaluation of programs and systems under the artificial heart program.

   Specifically, experiments on calves with electrically driven artificial hearts have been realized that have lived up to 36 days. To realize the importance of this, it must be stated that no other program and no other laboratory has been able to sustain a calf with an electrically driven total artificial heart for more than a few days.

6. Determined and evaluated performance of the bench model and began performance studies with the ERDA systems in experienntal animals during rest, standing and exercise.

   Techniques were investigated for determining cardiac output and other in vivo pumping performance parameters of the system using a NASA developed implantable data telemetry system. Specifically, some calves have been exercised on a treadmill. Blood chemistry and lung function are within normal limits. The calves had good appetites and continued to grow.

7. Prepared Final Report on Artificial Heart System Contract at the Institute. Provided results, conclusions and recommendations relaized during the contract.

In general, adequate and timely progress was made by the Institute in completing its assigned tasks under the contract. Figure III-I shows an overall schedule for the DOE Artificial Heart Program.

OVERALL SCHEDULE

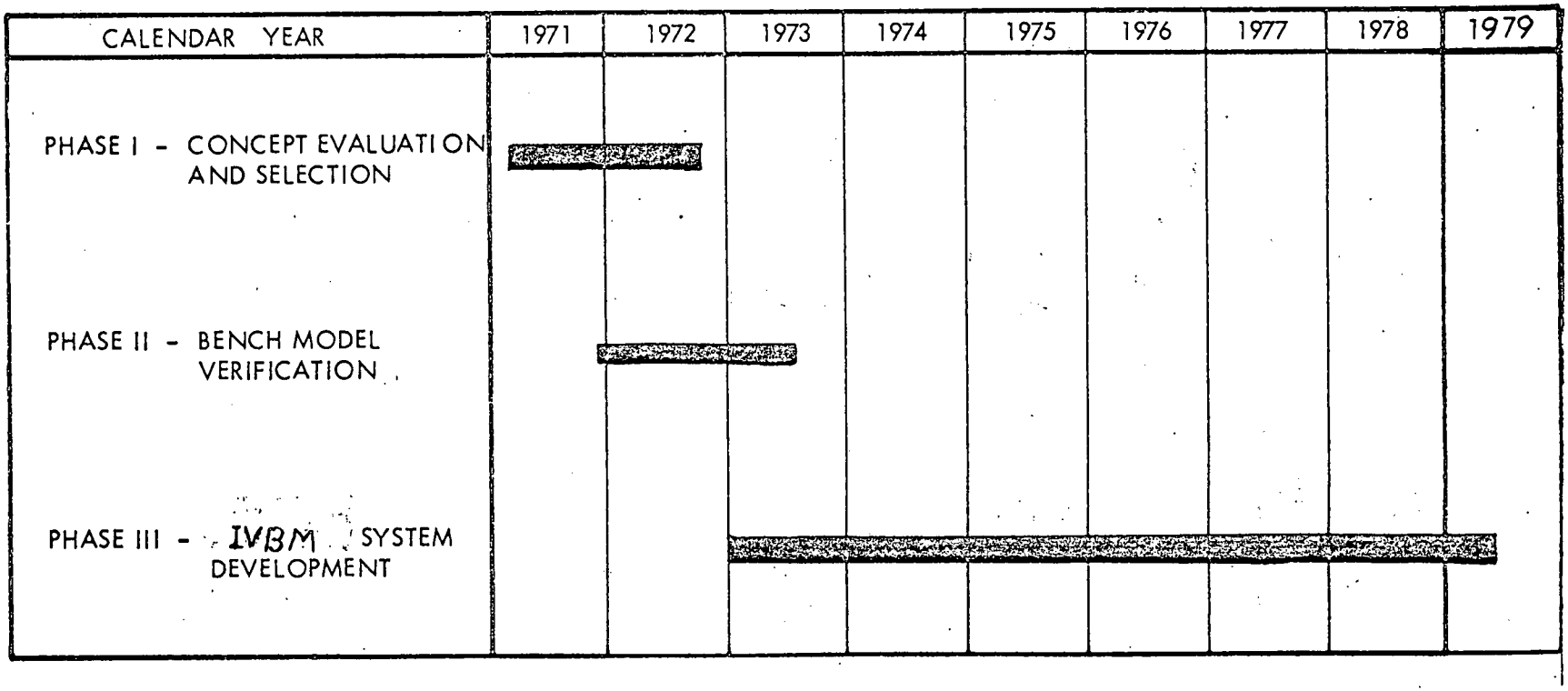


Figure III-I: Overall Schedule for the DOE Artificial Heart Program

IV: OVERALL PROGRAM GOALS FOR THE DOE ARTIFICIAL HEART PROGRAM

The basic goal of the original AEC Artificial Heart Program was to develop and construct an Artificial Heart System, powered by a plutonium-238 heat source, which could be successfully employed as an implantable total artificial heart system for animal experiments. Experiments and studies under the program were directed at eventually developing and evaluating a satisfactory system for total heart replacement in humans.

Criteria established early in the program as major development goals to be realized by a Prototype Artificial Heart System were as follows:

1. Isotope Inventory: "To establish and employ the minimum Pu-238 inventory for the heat source necessary for a practical operational system."

All of the inefficiencies in the artificial heart system are reflected in the radioactive isotope inventory. Thus, for a given amount of power to be delivered to the blood, the higher the system efficiency the lower the isotope inventory. And, as the isotope inventory is lowered, so are the potential annual and cumulative requirements for plutonium-238, the heat source cost, the amount of heat to be dissipated to the body, the recipient radiation exposure, and the population radiation exposure. The conclusion made was that the isotope inventory necessary for the system which might be used clinically in the 1980's could be equal to or less than 30 watts. If isotope inventory were the only criteria, at about 30 watts one could be confident about the practicability of a system.

2. Implantation Factors: "To establish and satisfy the physiological and biological requirements and constraints imposed upon the entire implantable system."

Primary among the numerous considerations grouped under the implantation factor heading were the weight, volume, and shape of the individual components of the system, e.g., the thermal converter and the blood pump. Studies with the IVBM System at the University of Utah have led to the judgment that the thermal converter as built was too large for accommodation in a human. The IVBM blood pump was also large but the prototype model (which was not built) appeared to be acceptable for human accommodation.

Waste heat from the converter could be dissipated through the converter surface into the tissue surrounding the converter and through the blood pumping mechanism into the blood circulating through the ventricles. In no case did the heat flux exceed 0.1 watt/cm^2 to tissue or 0.9 watt/cm^2 to blood.

Initial findings were that the system was capable of functioning continuously for some time before implantation - on the shelf in the fabrication facility after fueling and checkout, during packaging and shipping, on the shelf near the surgical facility. It could be constructed of materials that could be readily sterilized and biocompatible.

3. Operational Performance: "To design, test and evaluate the operational performance necessary for a potential long-term total heart replacement system."

The power required to drive the blood pump in calves was determined by the University of Utah. Mean peak blood flow rates of about 11 liters per minute were achieved at average mean aortic pressures of 120 mmHg and mean pulmonary artery pressures of 15 mmHg. This resulted in a blood pumping power for the total heart of 3.1 watts, 2.7 watts for the left ventricle and 0.4 watts for the right ventricle. This power level was projected as being sufficient to allow a 25 year old male weighing 68 kilograms to perform moderate activity.

A 10-year mean life for the system was initially established as the lifetime criteria. Wearout failure was defined by a probability curve with a three-sigma point at five years.

4. Environmental Impact: "To determine the total environmental consequences of such an artificial heart system and to attempt to develop a system acceptable by society."

A plutonium-238 powered artificial heart system might be fully acceptable from a technical viewpoint, yet, conceivably, be unacceptable for general usage because of its radiological implications. Of specific concern was the release of plutonium-238 into the biosphere and the possibility of uptake by man. This gave rise to two important practicability considerations. The first was that the heat source and system design should be such that there was complete containment of the plutonium-238 under all credible accident conditions throughout the proposed operational life of the device. The second recognized the very real possibility that accidents might occur in which the recipient might never be located and lead to an objective of 1000 years containment, a period sufficient to allow the Pu-238 to decay to about 1/3000 of its original value of radioactivity.

. Cost: "To determine the availability, potential demand and cost of such an artificial heart system with the goal of wide availability at acceptable cost."

To justify the continued development of an artificial heart system, there must be some assurance that it can eventually be made available in large numbers at a reasonable cost. To date, there has been little success in obtaining a final consensus on either a system cost or an annual operating cost (for the 1980's) that could be used as a measure of acceptability. In any event, costs are probably best represented on an annual basis assuming a fixed operating life for the system and must cover: leasing of the plutonium-238 and replacement of that which decays each year; amortization of the system (thermal converter, blood pump drive, ventricles, etc.) and the initial surgical procedures; and, the follow-up treatment. It was determined that the preliminary annual cost for an artificial heart would probably not exceed that associated with the use of an artificial kidney.

V: CARDIAC POWER REQUIREMENTS FOR A REFERENCE ADULT HUMAN

The actual power delivered to the circulating blood of an adult human can be deduced from various sources. Since a quasi-linear relationship between cardiac output and oxygen consumption has been established by several investigators (A.C. Guyton, E. Asmissen, M. Nielsen, O.L. Wade, J. M. Bishop, et al), power input to and output from the heart can be determined. Direct pressure, flow measurements are also possible for inferring normal cardiac performance. Also, the use of the standard equations for incompressible fluid flow permit the determination of power delivery for a given flow.

In the progress report dated April 15, 1972 submitted by the Institute to the AEC, the activity profiles of the standard reference man and woman defined by the Food and Agriculture Organization of the United Nations was used to describe the power requirements for an artificial heart. The description of the Reference Man and Reference Woman is given as follows:

> The Reference Man is 25 years of age. He is healthy, that is, free from disease and physically fit for active work. He weighs 65 kilograms. He lives in the temperate zone at a mean annual temperature of 10° C. He consumes an adequate well-balanced diet and neither gains nor loses weight. On each working day he is employed 8 hours in an occupation which is not sedentary, but does not involve more than occasional periods of hard physical labor. When not at work, he is sedendary for about 4 hours daily and may walk up to 1½ hours. He spends about 1½ hours on active recreation and household work. The Reference Man as defined above is assumed to require an average for the entire year, of 3200 (kilo) calories daily.
>
> The Reference Woman is a similarly healthy woman aged 25 years, and weighing 55 kilograms. She lives in the same environment as the Reference Man. She may be engaged either in general household duties or in light industry. Her daily activities include walking for about 1 hour and 1 hour of active recreation, such as gardening, playing with children, or nonstrenuous sport. The Reference Woman is assumed to require on an average for the entire year, 2300 (kilo) calories daily.

Table V-I shows the activity profile of the male along with the metabolic energy profile, cardiac output profile, right ventricular power profile, left ventricular profile and total heart power profile. Table V-2 gives the same information for the female. The basal metabolic rates were determined from Altman, P.C. and Dittmer, D.S., Metabolism, Federation of American Societies for Experimental Biology, Bethesda, MD, 1968.

Calculations of cardiac output for different types of activity based on metabolic and nutritional data in the literature, combined with the experimentally measured artificial heart efficiencies, indicate that the average power required by a 25 year old, 68 kg, 173 cm male human leading a relatively active life is 2.7 watts with a maximum power requirement during moderate exercise of 4.1 watts. For the 25 year old, 60 Kg, 165 cm female, the average power is 2.4 watts and the maximum power is 3.3 watts. In both the male and female, nutritional data indicate that the average power requirements of the artificial heart decrease slightly with age and increase slightly with body weight.

ACTIVITY, ENERGY, OUTPUT AND POWER PROFILES FOR MALE

(Age 25 years, Height 173 cm, Weight 68 kg)

ACTIVITY	DURATION Hours	RATE OF ENERGY UTILIZATION Kcal/min	CARDIAC OUTPUT L/min	POWER REQUIRED TO DRIVE ARTIFICIAL		
				RIGHT VENTRICLE Watt	LEFT VENTRICLE Watt	TOTAL HEART Watt
Sleep	8	0	6	0.33	2.22	2.55
Dressing, Etc.	1	2.12	9.03	0.50	3.35	3.85
Driving	½	1.62	8.32	0.47	3.08	3.55
Moderate Work	4	1.82	8.6	0.48	3.18	3.66
Walking	¼	3.12	10.5	0.59	3.90	4.49
Lunch	½	0.26	6.37	0.36	2.36	2.72
Walking	¼	3.12	10.5	0.59	3.90	4.49
Moderate Work	4	1.82	8.6	0.48	3.18	3.66
Driving	½	1.62	8.32	0.47	3.08	3.55
Moderate Exercise	1	3.82	11.5	0.65	4.25	4.90
Dinner	1	0.26	6.37	0.36	2.36	2.72
Relaxation	3	0.82	7.17	0.40	2.65	3.05

TABLE V-I

Aortic Pressure - 100 mmHg
Pulmonary art. pressure - 15 mmHg
Basal Metabolic Energy - 1700 Kcal/day

Artificial heart efficiency - 60%
Average power requirement - 3.23 watt
Total Metabolic Energy - 3294 Kcal/day

ACTIVITY, ENERGY, OUTPUT AND POWER PROFILES FOR FEMALE

(Age 25 years, Height 165 cm, Weight 60 Kg)

ACTIVITY	DURATION Hours	RATE OF ENERGY UTILIZATION Kcal/min	CARDIAC OUTPUT L/min	POWER REQUIRED TO DRIVE ARTIFICIAL		
				RIGHT VENTRICLE Watt	LEFT VENTRICLE Watt	TOTAL HEART Watt
Sleep	8	0	6	0.33	2.20	2.53
Dressing, Etc.	1	2.32	9.32	0.52	3.46	3.98
Domestic Work	5	0.5	6.72	0.37	2.47	2.84
Lunch	1	0.26	6.37	0.36	2.36	2.72
Driving	¼	1.62	8.32	0.46	3.08	3.54
Walking	1	1.86	8.66	0.48	3.22	3.70
Driving	¼	1.62	8.32	0.46	3.08	3.54
Domestic Work	2	0.5	6.72	0.37	2.47	2.84
Dinner	1	0.26	6.37	0.36	2.36	2.72
Domestic Work	½	0.5	6.72	0.37	2.47	2.84
Exercise	1	2.0	8.86	0.49	3.29	3.78
Relaxation	3	0.5	6.72	0.37	2.47	2.84

Aortic Pressure - 100 mmHg
Pulmonary Art. Pressure - 15 mmHg
Basal Metabolic Energy - 1480 Kcal/Day

Artificial Heart Efficiency - 60%
Average Power Requirement - 2.9 watt
Total Metabolic Energy 2304 Kcal/day

TABLE V-2

VI: DESIGN AND CONSTRUCTION OF THE VENTRICLES

In compliance with contract requirements the design and construction of the blood handling parts of the blood pump was undertaken. This blood pump was designed as a bench model system but was subsequently found to be suitable for limited in vivo experimentation. Westinghouse Astronuclear Laboratory was responsible for the design and construction of the pump drive mechanism. To insure there would be no difficulties in interfacing the ventricles and pump drive mechanism, control dwellings were supplied which dictated the dimensions necessary to insure proper fitting of the ventricle and pump drive mechanism as shown in Figure VI-1. From Figure VI-1 it can be seen that the diaphragm is attached to the pusher cup by means of a rubber tab extending from the diaphragm and locked to the pusher cup using roll pins. The soft-shelled dome of the ventricle is attached to the blood pump by two grooves and banded with wire. Figures VI-2. and VI-2. show a photograph and an outline drawing of the bench model blood pump, excluding blood connectors. Under the constraints of size and attachment to the bench model blood pump, a series of fit trials in dead calves were performed with several configurations of inflow and outflow connectors. These models were made of dental stone with the same dimensions as the bench model blood pump but including connectors. The animal was sacrificed and the chest opened midsternally. The natural heart was excised, leaving as much of the aorta and pulmonary artery as possible. The atria were also left intact. Woven Dacron grafts were sewn to the arterial vessels, the aorta graft being 3 cm in length, the pulmonary graft being 9 cm in length. Atrial cuffs of Silastic and fabric with a wire tie were sewn to the atria for the purpose of attaching the heart. After this preparation, which is very similar to an actual artificial heart implantation preparation, the models were tried for fit. The final connector configuration was then determined by repetition of this procedure until it yielded a configuration of connectors that was considered practical and yet could be expected to produce good hemodynamic results.

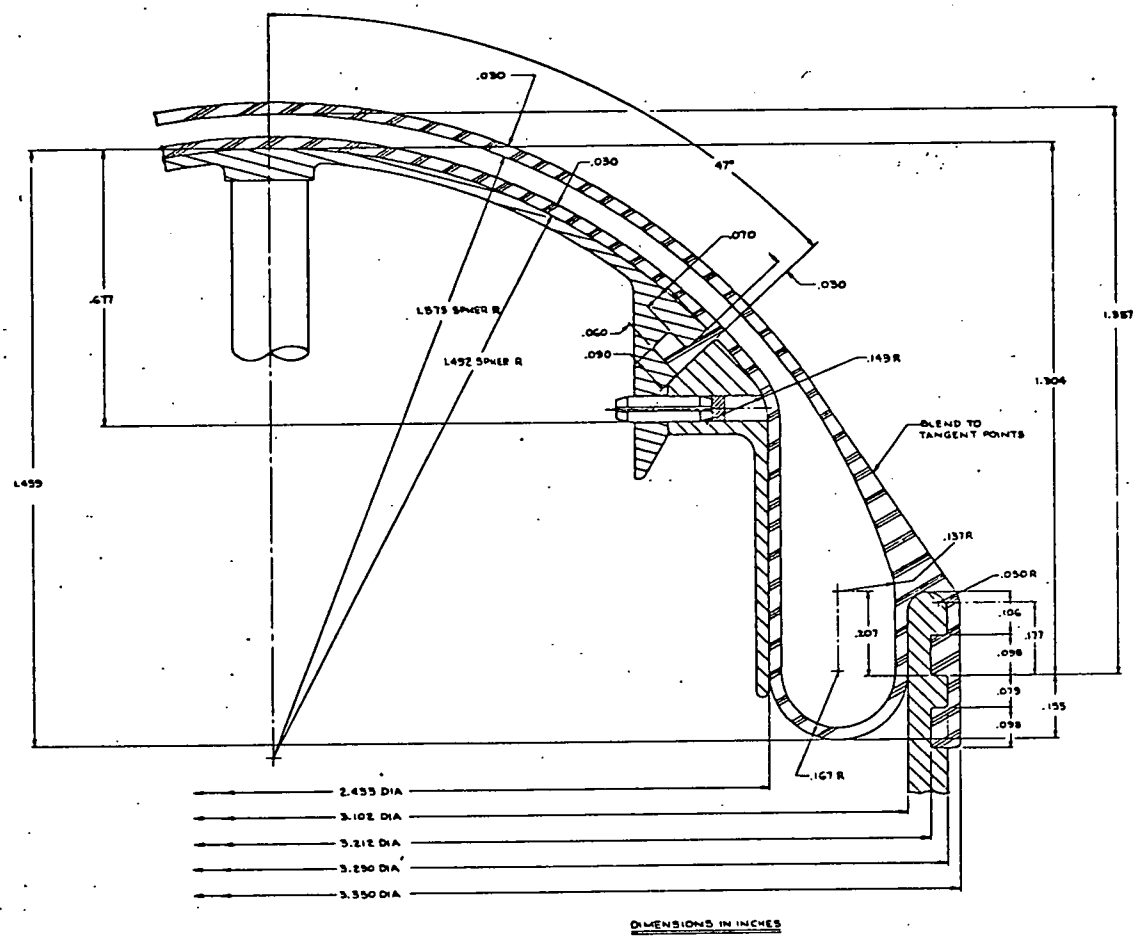
The design of the diaphragm consisted merely of insuring that its dimensions were compatible with the blood pump dimensions.

The experience gained in this laboratory has shown that Silicone rubber is a suitable material for fabrication of the bench model ventricles shown in Figure VI-I. This material has the advantage that it is quasi-blood compatible and lends itself readily to construction facilities available in the laboratory. For the purpose of manufacturing diaphragms and soft-shelled domes from silicone rubber, aluminum molds were fabricated. These molds are suitable for the manufacture of ventricles either from reinforced Silastic or from nylon fabric sealed with a Silastic dispersion coating. These molds should also be suitable for fabrication of ventricles using urethane and dipping process. Figure VI-3 shows photographs of the left and right ventricle molds.

Previously in other artificial heart implantations by the Institute for Biomedical Engineering at the University of Utah, the left and right ventricles were separate and there was adequate space for connections to the blood pump and vessels to be made by double wound wire or suture connections. An actual implant of the AEC blood pump using the double wound wire connection demonstrated the great difficulty encountered in

completing such a connection procedure when both ventricles are joined together. Therefore, a quick connect system was conceived which would reduce the surgery time and make the implantation easier. Using such a quick connect system, the arterial grafts and atrial cuffs are sutured into position and the blood pump is then inserted. Proper valve alignment between the male and female connection is made by squeezing the rings together. The female snap ring locks into the male ring and provides a positively tight connection. Figure VI-4 shows the quick connect system. Figures VI-5 and VI-6 show a complete assembly and molds for the system. A Silastic cuff on the female side of the quick connect system is molded into the ventricles during fabrication. A suture cuff is attached to the male rings shown in the right of Figure VI-4 and the cuff is sutured during surgery to the atria.

The initial quick connect system required precision machining and close attention to dimensional fit and some problems were encountered in dimensional variations occurring in Silastic parts during assembly and autoclaving. However, the latter polycarbonate, injection molded quick connect system has been employed successfully in over 100 implants of the blood pump in calves by the Institute.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.050R
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.098
.207
.079
.155
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.167R
2.455 DIA
3.102 DIA
3.212 DIA
3.290 DIA
3.350 DIA
DIMENSIONS IN INCHES

FIGURE VI-1

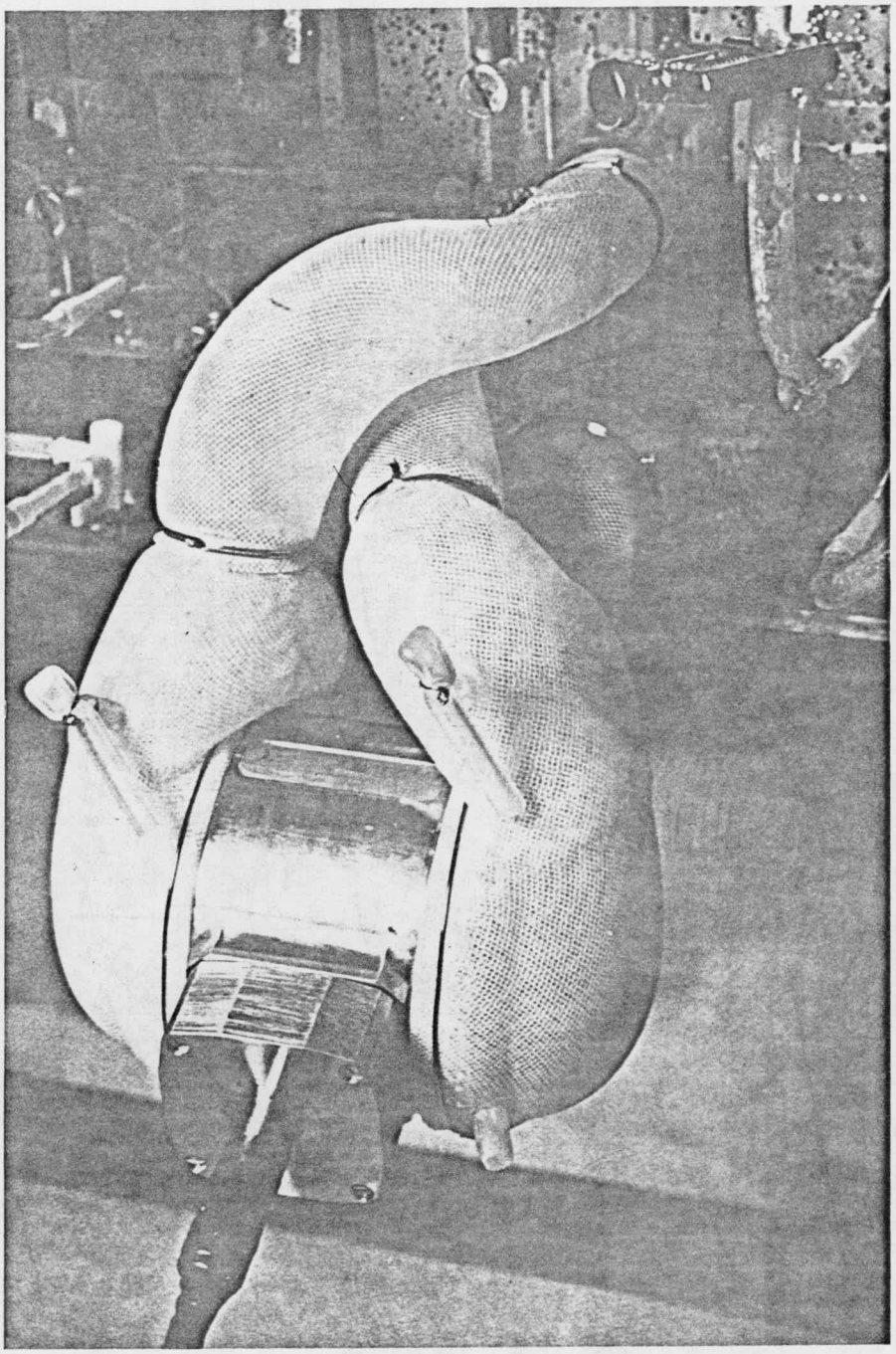


Figure VI-2.1
In vitro testing of AEC Bench Model Blood Pump on a mock circulation system

IMPLANTABLE BLOOD PUMP

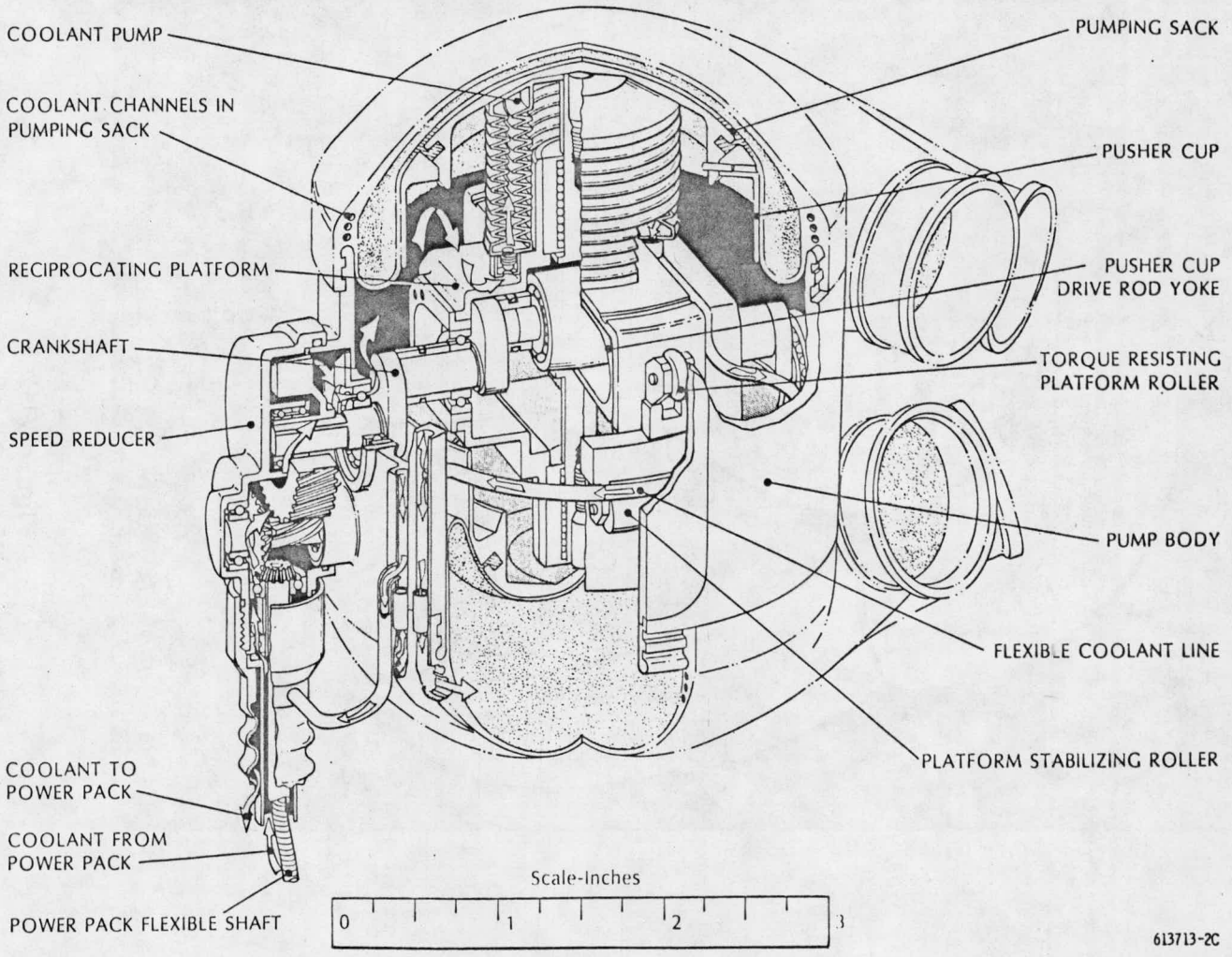
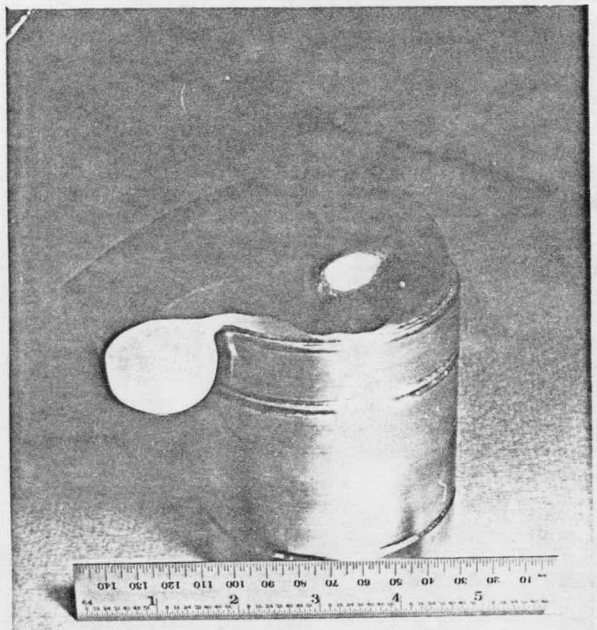


Figure VI-2.2



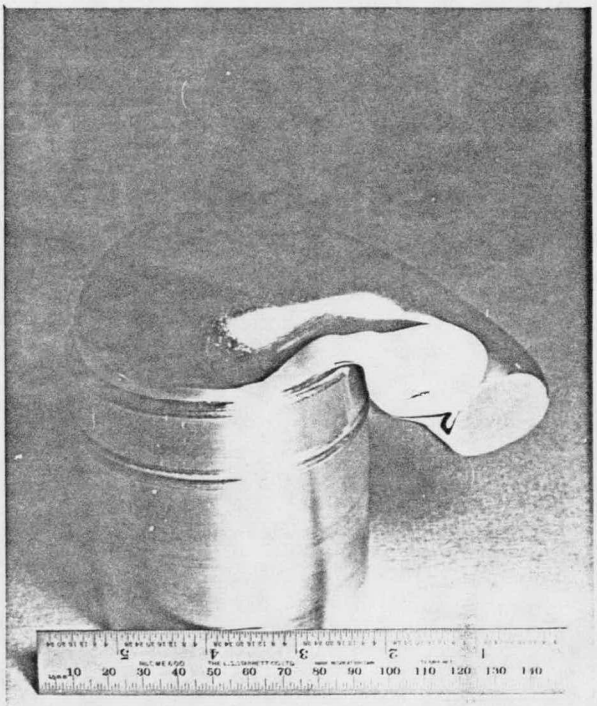
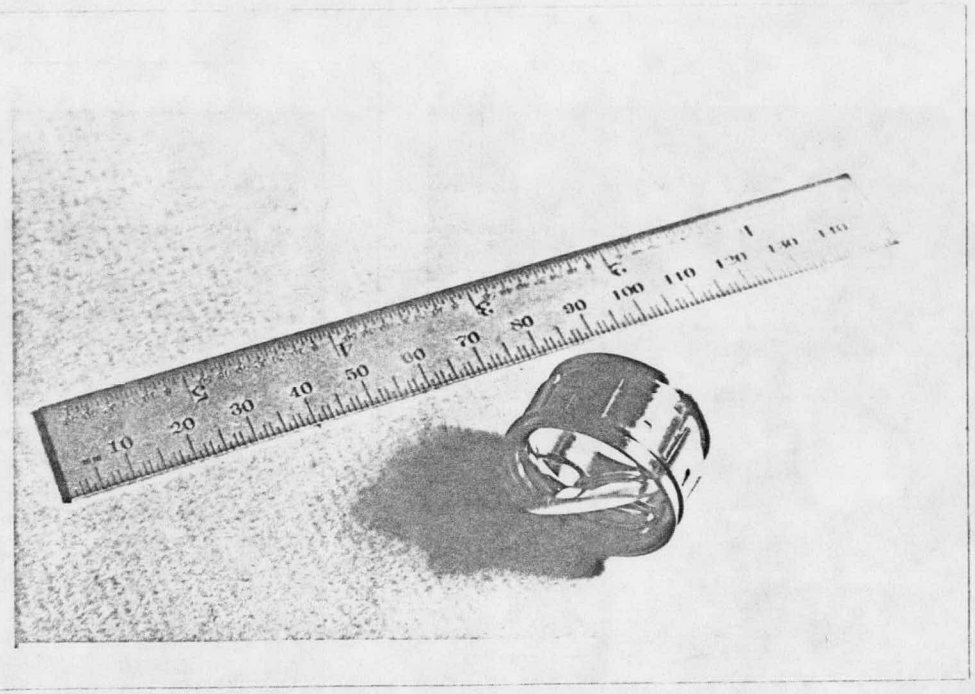


Figure VI-3: Photographs of housing molds.



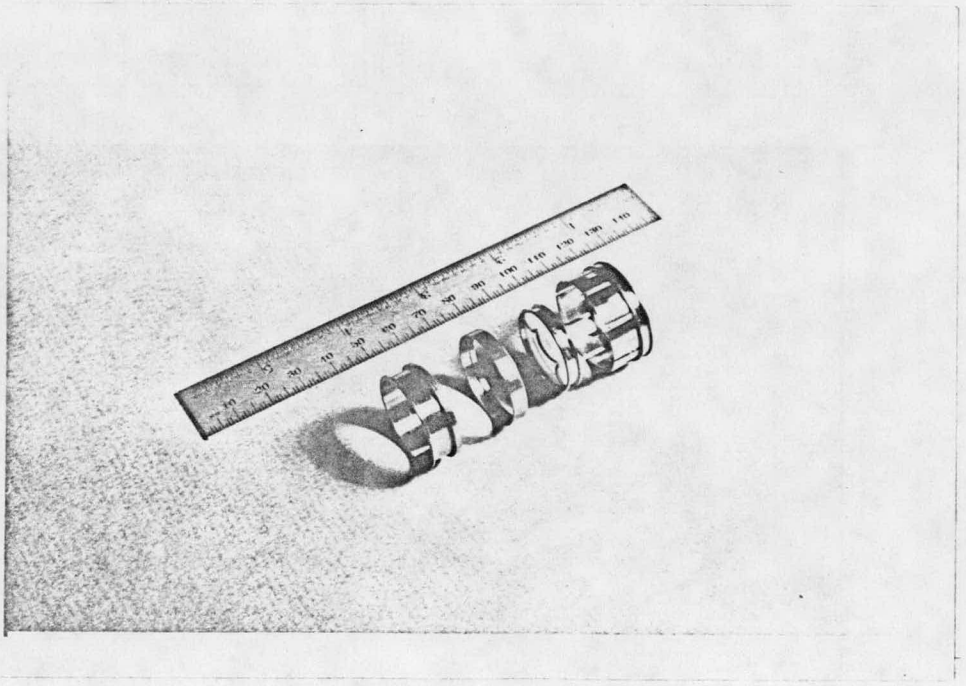


Figure VI-4: Photographs of quick connect system.

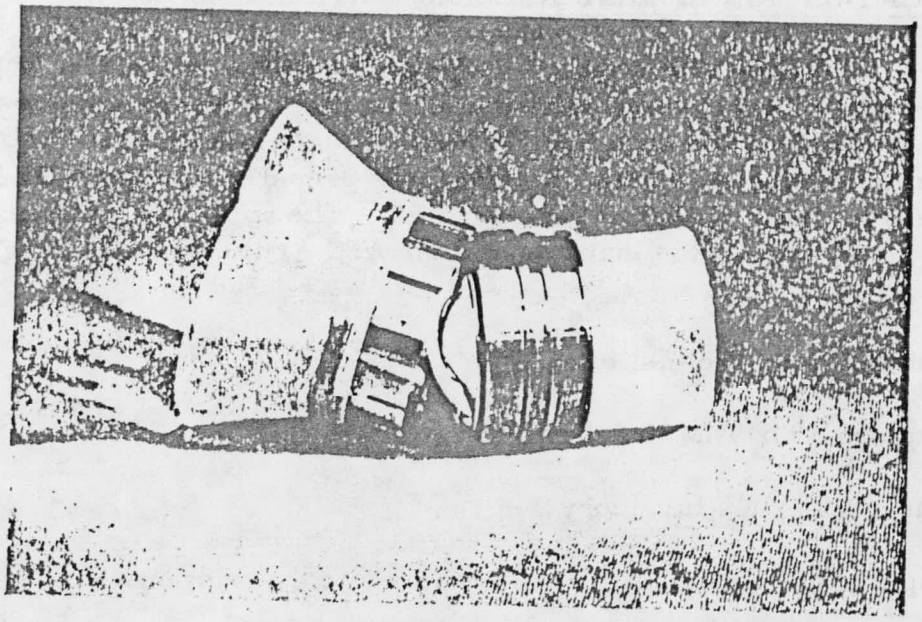


Figure VI-5
Complete Quick Connect System

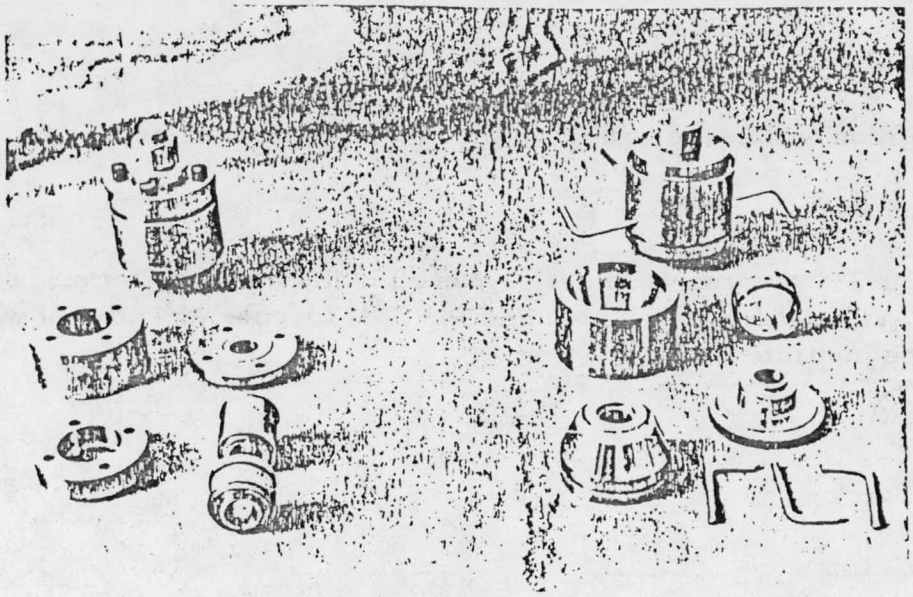


Figure VI-6
Stainless Steel Mold Set for Making Silastic Quick Connect Parts

VII: APPLICATION FOR SPECIAL NUCLEAR MATERIAL LICENSE

In order for the Institute of Biomedical Engineering at the University of Utah to receive, store and utilize Pu-238 encapsulated sources used as power supplies for the thermal converter, an application for a Special Nuclear Materials License (as Amendment Number 6 to the University of Utah SNM 663) was prepared and submitted to the Division of Material Licensing (DML) of the U.S. AEC. The application provides detailed information and data on the institute and the AEC Artificial Heart Program, as indicated below:

1. General information on the Institute.

2. Duration requested for SNM license.

3. Special nuclear materials inventory.

4. Activity proposed under the SNM license and a site description.

5. Administration and technical qualifications.

6. Health physics equipment facilities.

7. Nuclear criticality evaluation.

8. Hazard assessment and maximum credible accident evaluation.

9. Shipment of SNM.

10. Detailed description and usage of SNM in the artificial heart system.

11. Record maintenance.

However, the Pu-238 sources were not delivered to the Institute because of programmatic changes in the Artificial Heart Program and the SNM License Amendment was allowed to lapse by the Institute.

VIII: IMPLANTATION OF INERT MODELS OF THE THERMAL CONVERTER IN THE ABDOMENS OF CALVES

During the period of August 1972 to December 1973, inert models of the AEC radioisotope powered thermal converter were implanted and studied in a total of eight calves (five normal calves at an average weight of 99 kg, or 218 lbs, and three dwarf calves at an average weight of 130 kg or 287 lbs) to determine the calf's tolerance as an experimental animal to the chronic effects associated with the weight and size of such a device implanted in the abdominal region.

The basic construction material for all of the models (except the aluminum model - Implant No. II) was Dow Corning Silastic "D" RTV mold making rubber. Pertinent data on these inert models are as follows:

Inert Model without Gear Housing Bus and Simulated Flexible Drive Shaft

Material: Dow Corning Silastic "D" mold making rubber
Volume: 860 cc (avg.)
Weight: 1200 g (avg.)
Density: 1.39 g/cc (avg.)
Covering: Dacron net reinforced Silastic with a Dacron velour suture cuff

Inert Model with Gear Housing Bus and Simulated Flexible Drive Shaft

Material: Dow Corning Silastic "D" mold making rubber
Volume: 938 cc (avg.)
Weight: 2235 g (avg.)
Density*: 2.38 g/cc (avg.)
Covering: Dacron net reinforced Silastic with a Dacron velour suture cuff

One inert model of the thermal converter was fabricated from type 5052 aluminum (See Implant No. II).

Because of the time and expense associated with fabrication of the aluminum model, only one implant using an aluminum model was made.

The actual flexible drive shaft employed to transmit power from the thermal converter to the blood pump was simulated in these experiments by a one-quarter inch diameter Silastic tube about ten inches in length, which was stiffened internally with wire and solid polyethelene rod to simulate the actual drive shaft. The end of the simulated drive shaft, which was blunted and sealed to prevent puncture of vital organs and to exclude body fluids, was passed through the diaphragm wall of the calf and into the thoracic cavity near the heart.

---

*Increase of the inert model density over Silastic rubber (1.39 g/cc) was accomplished by internally weighing the model with a heavy inert metal. This density increase was felt necessary in light of Westinghouse's (WAL) proposed converter weight increase to about 2 kilograms.

Figure VIII-1 is a photograph of the inert model with the gear housing bus and simulated flexible drive shaft. The Silastic covering can be seen and the Dacron velour suture cuff is shown outlining the upper side of the inert model.

The surgical procedure for implantation of the inert model is given in Table VIII-1. Implant models No. I and II did not have a bus and flexible shaft. Modifications and improvements in the surgical protocol and procedure were made during the implantation experiments. Surgical procedure for Implant No. VIII was briefly as follows. After the necessary surgical preparation of the calf, a 12 cm incision through the abdominal skin at the right paramedian was made. A tunnel was then created between the skin and abdominal muscle wall from the incision line to the vicinity of the linea alba which was separated from the peritoneum. The inert model with the gear bus up and flexible shaft aligned towards the thorax was inserted between the peritoneum and the linea alba with the engine placed slightly left of the abdominal midline. The flexible shaft was inserted into the thorax to the right of the heart through a puncture made in the abdominal wall near the xiphoid. The diaphragm puncture was then sutured around the flexible shaft. The sewing cuff encircling the inert model was then sutured to the linea laba, and the abdominal wall incision was then closed. Because the diaphragm was punctured to introduce the flexible shaft into the thorax, entrained air had to be removed to correct the pneumothorax.

Table VIII-2 presents a synopsis of data on the eight calves which had inert models implanted in the abdominal region. The inert model was placed inside the peritoneal cavity in Implant No. I to evaluate accommodation there. However, a draining sinus tract developed on the left abdominal wall directly under the implanted model and the animal was sacrificed on November 29, 101 days after implantation. The pathologist's report on Implant No. I was as follows:

> "Autopsy performed November 29, 1972 on a dwarf Hereford Heifer (female) calf in which an RTV AEC inert model had been implanted on August 21, 1972. Because of a draining sinus tract on the left abdominal wall at the most dependent portion in the standing animal, the above referenced calf was sacrificed on November 29, 1972.
>
> The drainage was typical of rumen content with the characteristic odor of Sphaerophorus necrophorus infection. Presenting into the tract was the finger of the model. The cylindrical edge had created pressure necrosis of the skin and underlying tissues including the rumen wall. The skin and subcutaneous tissues at this localized site were infected.
>
> The entire model was encased in a very dense fibrous capsule continuous with the interior of the rumen and was filled with rumen fluids. These fluids and microflora had dissolved the sutures attaching the model to the abdominal wall.
>
> This model was implanted within the peritoneal cavity of a dwarf calf, and it is theorized that the model which was indirect contact with the anterior ventral sac of the rumen created pressure necrosis of the rumen wall. This was a result of the abnormal confirmation and physiology of the experimental animal selected.

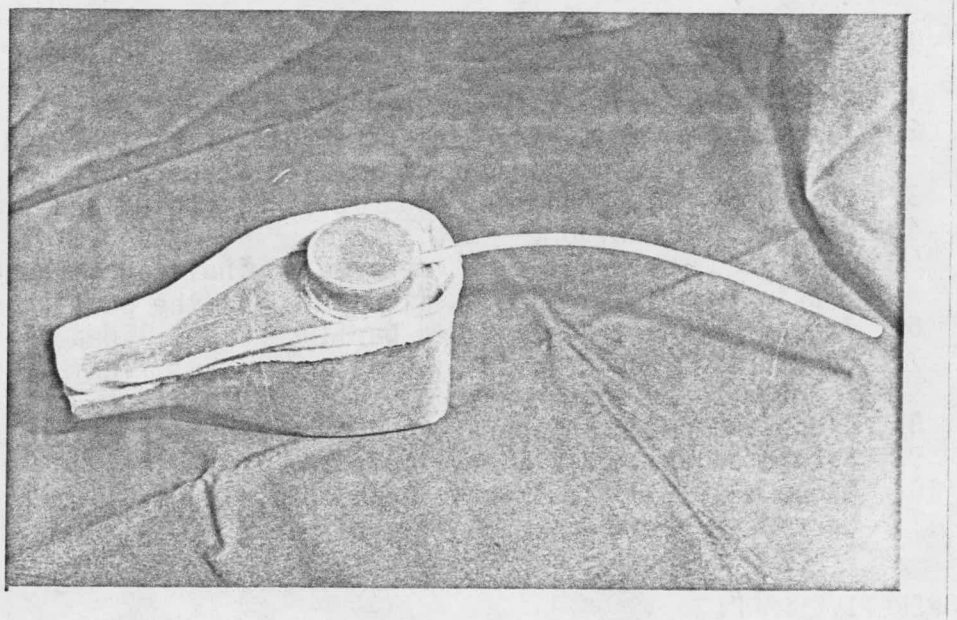


FIGURE VIII-1: Photograph of R.T.V. Engine Model.

TABLE VIII-1

PROTOCOL

IMPLANT AEC ENGINE

PURPOSE: To determine chronic effect of the weight and large size of AEC nuclear engine model

PERSONNEL:

Surgeons	Model Manufacturer
Anesthesia	Photography
Instruments	

ANIMAL: Normal Calf

ENGINE MODEL: RTV model with density corrected to AEC engine density, Silastic covered with Silastic and Dacron sew tabs

OPERATIVE PROCEDURE:

1. Induce anesthesia with Brevane and Atropine (2 mg).
2. Place animal on table. Insert endotracheal tube and stomach tube. Restrain and connect to Bird Respirator.
3. Prep cervical, abdominal and umbilical region and drape.
4. Connect EKG monitor.
5. Open abdominal wall-right paramedian incision through the skin tunnel to and open linea alba to the peritoneum.
6. Insert engine model between peritoneum and linea alba.
7. Puncture diaphragm near xiphoid and insert flexible shaft into thorax near heart.
8. Close and suture diaphragm puncture around flexible shaft.
9. Suture engine model sewing cuff to linea alba.
10. Close incision, administer Combiotic, 10 ml., locally at incision.
11. Correct pneumothorax.

POSTOPERATIVE CARE:

1. Place animal in clean bedded inside stall.
2. Antibiotic - Combiotic, 10 ml/day, I.M. for 4 days.
3. Allow one week recovery at Bldg. 512.
4. Move to the South 40.

TABLE VIII-2

IMPLANT OF INERT MODELS OF THE AEC THERMAL CONVERTER

IMPLANT NO. & DATE	MODEL DESCRIPTION (Basic model form supplied by WAL)	CALF DESCRIPTION
I 21 Aug. 1972	Material: Dow Corning Silastic "D" Volume: 860 cc Weight: 1200 gr Density: 1.39 g/cc Covering: Dacron net reinforced Silastic with a Dacron velour suture cuff	Dwarf - Hereford Heifer (Red) 130 kg (287 lbs.) Sacrificed on 29 Nov.1972 101 days' survival Model implanted inside peritoneal cavity - stomach penetrated
II 25 Sept. 1972	Material: Aluminum with internally adjusted density Volume: 880 cc Weight: 1950 gr Density: 2.22 gr/cc Covering: Same as I	Normal-Hereford Heifer (Black) 95 kg (210 lbs.) Implanted animal terminated on 12 Dec. 1973 - 443 days survival
III 26 Oct. 1972	Material: Same as I except internally weighted Volume: 890 cc (includes a buss for gear housing and a 1/4 inch diameter, 9-inch long stiffened Silastic tube to simulate the flexible drive shaft Weight: 2190 gr Density: 2.46 gr/cc Covering: Same as I	Dwarf - Hereford Heifer (Red) 128 kg (273 lbs.) Sacrificed on 24 Dec.1972 60 days' survival Opening of incision
IV 27 Nov. 1972	Material: Same as III Volume: Same as III Weight: 2195 gr Density: 2.46 gr/cc Covering: Same as I	Dwarf - Angus Heifer (Black) 132 kg (292 lbs.) Sacrificed on 24 Jan.1973 59 days' survival Opening of incision
V 17 Jan. 1973	Material: Same as III Volume: Same as III Weight: 2210 gr Density: 2.48 gr/cc Covering: Same as I	Normal - Hereford Heifer (Black) 97 kg (214 lb.) Model removed on 23 Aug. 1973 (218 days' implant) Some local infection but acceptable.

Table VIII-2 Implant of Inert Models of the AEC Thermal Converter (cont'd.)

IMPLANT NO. & DATE	MODEL DESCRIPTION (Basic model form supplied by WAL)	CALF DESCRIPTION
VI 31 Jan. 1973	Material: Same as III Volume: 985 cc Weight: 2342 gr Density: 2.48 gr/cc Covering: Same as I	Normal - Holstein Bull (White) 115 kg (254 lbs.) Sacrificed on 2 Feb 1973 Right pneumothorax, collapsed lung
VII 8 Feb. 1973	Material: Same as III Volume: 985 cc Weight: 2238 gr Density: 2.27 gr/cc Covering: Same as I	Normal - Angus Heifer (Black) 91 kg (201 lb.) Model removed on 20 Apr. 1973 71 days' implant Local infection
VIII 20 Feb. 1973	Material: Same as III Volume: 985 cc Weight: 2240 gr Density: 2.27 gr/cc Covering: Same as I	Normal - Holstein Steer (White) 96 kg (207 lb.) Model removed on 5 July 1973 135 days' implant Local infection

Future inert model implants should be made exterior to the peritoneum which protects the rumen wall from pressure necrosis. The intact peritoneum allows the natural mobility of the rumen to distribute these critical pressures over a larger area."

Implant No. II was made on September 25, 1972 in a normal Hereford Heifer calf employing an inert aluminum model which was internally weighted to approximate Westinghouse's recently announced engine weight requirements of approximately 2 kilograms.

An X-ray of the abdominal region of this calf, taken August 30, 1973 showed that the inert aluminum model was still in position and no external signs of infection or trauma at the implant site were evident. The sutured incision was completely healed and only slight scar tissue was evident.

Implants III and IV were both conducted in dwarf calves and proved unsuccessful. Initially, during the implant program, dwarf calves were chosen because of minimal growth expected and thus small anatomical changes expected during the anticipated experimental evaluation period. However, the attempted use of three dwarf calves as experimental animals for inert model implant was not successful. All implanted dwarf calves developed serious complications related to the implant and had to be terminated. The model in Implant No. I was placed inside the peritoneal cavity but a draining sinus tract developed on the left abdominal wall. Two other dwarf calves, Implant Nos. III and IV, received implants but because of the very large abdomen characteristic of dwarf calves and their persistent tendency to bloat (chronic ruminal tympany), severe tension was created across the sutured incision site and eventually under the cycling stress of the moving animal, the incision opens permitting the invasion of bacteria and subsequent infection which ultimately requires termination of the preparation.

The pathology report on Implants Nos. III and IV went as follows:

"These calves survived 60 days with an inert model of the AEC thermal converter implanted in the ventral abdominal wall. They were selectively uthinized at 60 days because of infection and sinus tract drainage from the model site to the exterior at the posterior end of the midline incision. The amount of drainage was minimal and the odor indicated infection with Sphaerophorus necrophorus, a common saprophyte that gains access into the tissue of cattle housed in barnyard environments. In both cases, the model was totally encased within a fibrous connective tissue coating and the sinus tract traversed the line of surgical incision. It appears that the large abdomen characteristic of dwarf calves and chronic ruminal tympany does not make these animals conducive for the housing of this particular implant within the ventral abdominal wall."

As a result of the experience with Implants III and IV two changes were incorporated in the remaining implant experiments. The use of dwarf calves for implants was discontinued and normal calves were used throughout the remainder of the program.

Also, the abdominal incision was made to the right of the abdominal midline. The incision opening was then tunneled toward the midline, and the linea alba was excised down to the peritoneum where the model was implanted slightly to the left of the midline. This procedure allowed an overlapping of the model during surgical closure, and, thus, eliminated direct contact and attendant stress upon the suture line.

On January 17, 1973 an inert model implant (Implant No. V) was made in a normal Hereford Heifer calf. The surgical procedure was successful and the calf appeared to tolerate the implant well. However, after about six months local swelling appeared around the implant.

Careful inspection showed that the abdominal incision was closed and essentially healed; however, entrained fluid surrounded the model and internal infection was suspected.

On August 28, 1973, 218 days after implant of the engine, the model was removed from the calf and the animal was salvaged.

The pathologist's report on Implant No. V is as follows:

> "This model was encased in a heavy fibrous sac filled with non-odorous pus. There was no tract to the exterior and no evidence of bacteria. The Silastic housing of the RTV had leached out. These products are necrotoxic and created what is called a 'sterile abscess.' This was confirmed on histopathology."

The pathologist's report on an abdominal tissue biopsy taken near the model implant was as follows:

> "There is a heavy layer of subdermal connective tissue approximately 1 cm thick which contains varying degrees of vascularization and a small amount of fibrin deposition adjacent to its intersurface which was apparently lying adjacent to the engine implant. Other than the heavy fibrous capsule, there appears to be very little damage to the overlying dermis or epidermis. There are a few inflammatory cells surrounding some of the small vessels in the area immediately adjacent to hair follicles in the dermis and a few focal areas of mild scab formation are noted on the surface of the intact epithelium."

It is significant to observe from this report that after 218 days with the model implanted, although some vascularization with fibrin deposition occurred adjacent to the implant, the adjacent tissue suffered very little damage as a result of the implant.

Implant No. VI received an inert model implant on January 31, 1973 but two days later was found to have acute pulmonary impairment. An autopsy made after sacrifice of the animal indicated a collapsed right lung resulting from a right pneumothorax. Apparently, air admitted into the pleural cavity when the diaphragm was punctured to introduce the flexible shaft into the thorax was not adequately eliminated by post-operative procedures, or possibly air entrained around the inert engine was able to

enter the thorax through an inadequately closed penetration of the diaphragm made for the flexible shaft. However, physical examination of the closure did not confirm this suspicion. Regardless of the cause of the pneumothorax, the loss of the animal was not directly attributed to the presence of the inert model.

Implants Nos. VII and VIII were terminated due to the development of local infection in the vicinity of the sutured abdominal incision. Implant No. VII was terminated after 71 days and Implant No. VIII had the inert model removed from the abdomen after 105 days. This animal was salvaged and the abdominal infection contained and later eliminated.

The pathologist's report on Implants VII and VIII was as follows:

> "Evidence of purulent supuration in the immediate vicinity of the implanted inert model in both calves. It is conjectured that microorganisms gained entrance via 'thru and thru' silk sutures closing the abdominal incision. Perhaps a suturing procedure employing the separate layer technique would eliminate this avenue of microorganism entrance."

During the inert model implant studies the following observations were made:

Initially it was believed that dwarf calves would be desirable experimental animals because of their minimal growth and small anatomical change anticipated to long term experimental studies. The three dwarf calves employed in the implant study failed to satisfactorily retain the implanted model and the pathologist, a veterinarian, concluded that abdominal implants of the model in the vicinity of the linea alba were inadvisable. The dwarf developed a characteristically enlarged abdomen concomitant with chronic rumenal tympany.

The location of the model between the peritoneum and linea alba and the required incision for inserting the model resulted in certain problems in the ambulatory animal. The great weight of the abdominal region applied high stress to the sutured incision, as was apparent from the high loss rate of animals through incision opening and infection. This situation was subsequently improved somewhat by making the incision at some distance from the model location and then tunneling between the skin and the peritoneum to the implant position. This procedure avoided direct contact of the model with the incision site.

In several implants infection developed around the sutured incision. The pathologist conjectured that microorganisms gained entrance via the "thru and thru" suture technique, employed to close the incision. He suggested that future implants employ the "separate layer suture technique" to reduce this infection route.

On September 25, 1972, an inert model of the AEC thermal converter was implanted into the abdominal cavity of a Hereford calf. This model was unique from the other models that were implanted in that it was a highly polished, milled aluminum model which was coated with reinforced Silastic and had a suture cuff along the edge

for attachment in the abdomen. Noteworthy was the fact that this model was implanted just subperitoneal to the left of the umbilicus and near the coastal arch anteriorly. All muscle layers were then sutured and the skin closed. The calf was housed at the Institute's research farm in Granite, Utah. The calf's recovery was uneventful. It was necessary once to palpate the calf's stomach to verify the presence of the model since it was not obvious from external appearance.

On December 11, 1973 (443 days after implantation) this Hereford Heifer was terminated to evaluate the effects of the long term implantation of the model. At autopsy the model was very well encapsulated by a white fibrosis connective tissue capsule which completely surrounded the Silastic coated aluminum model. There were no discolorations, no signs of infection at any time during the course of this experiment. The interior of the rumen and reticulin which came in constant contact with the model through the peritoneum was remarkably clear and on external appearance the rumen and reticulin showed no sign of inflammation or peritonitis. On opening the Silastic encasement, the highly polished aluminum model retained its polished surface and it appeared that no body fluids had gained access to the aluminum surface. It is well known that any body fluids in apposition to aluminum causes immediate oxidation of the aluminum with severe black precipitates. On microscopic examination, the tissue capsule formed around the Silastic was composed of dense fibrosis connective tissue, very healthy, with no indication of foreign body reaction or infection.

This experiment demonstrated that a healthy calf can tolerate and carry the AEC thermal converter configuration for periods of up to 15 months or more with no untoward reactions. Items which made this particular experiment successful in the series of inert thermal converters implanted are:

1. The model was implanted within the abdominal cavity immediately beneath the peritoneum. All other models were implanted either subcutaneously or within the muscle sheets.

2. This model was made of highly polished, milled, aluminum, drilling and weighted to the correct weight distribution, whereas other implants were of room temperature vulcanizing rubber (RTV). The question thus arose, was there some material in the RTV rubber that diffused through the Silastic, creating the untoward tissue reaction observed in that group of experiments?

3. The fact that several of the RTV model implantations were carried out while the RTV rubber was still hot due to autoclaving may have contributed to premature termination of some of these experiments.

Conclusions that were reached at the close of the inert model implant experiments were that the thermal converter could be successfully implanted in the abdominal region in the vicinity of the linea alba. The average survival time of the eight calves receiving implants was about 128 days. Furthermore, Implant No. II which received the aluminum model, accommodated to the implant very well. Since those animals initially receiving the total system implant of both the blood pump and power supply (electric or nuclear) will be confined to a cage and not ambulatory, stresses induced by the system's bulk at the suture site will be small and controllable.

IX: SELECTION OF VALVES FOR THE ERDA BLOOD PUMP

A critical component of the ERDA Blood Pump is the choice of a practical but optimum valve. Most in vivo testing under the contract employed two or more Bjork-Shiley valves because of their clinical acceptance for humans. However, since the contract year 1977, most in vivo experiments preserved the two natural inflow valves of the experimental animal which provided a significant improvement of pump performance evidenced by lower pumping power requirements, increased cardiac output at similar conditions and probably less blood damage. Other natural valves (hetrographs), viz. the procine valves, have been tested in vitro in an ERDA ventricle in the left inflow position, the left inflow and outflow position together and the left outflow position. Preliminary conclusions are that pulmonary arterial and venous pressures are not significantly affected over Bjork-Shiley valve conditions. However, porcine valves are small and these tests may not be indicative of performance that might be obtained with larger natural valves.

Effect of Pumping Rate and Arterial Pressure

The effects of pumping rate on the cardiac output is shown in Figure IX-1. Observe that for pumping rates between 110 to 130 bpm that output is essentially unaffected by atrial pressure variation in the range -5 to 5 mm Hg. However, for atrial pressures above -5 mm Hg the cardiac output increases with increased pumping rate.

Effects of arterial pressure change on cardiac output were investigated by doing two tests from the base line: one at an outflow pressure of 70 mm Hg and one at an outflow pressure of 130 mm Hg. For decreased outflow pressures cardiac output is slightly affected by arterial pressure (See Figure IX-2). However, for increased outflow pressure there is a slight decrease in cardiac output. Maximum slopes of the function curve remain essentially the same throughout the changes of arterial pressure.

Valve Size

The present design for the blood pump specifies a 29 mm size Bjork-Shiley valve at the inflow. It is believed that this valve gives superior performance over the 27 mm size. In order to verify this belief a test was made to compare changes in cardiac output when decreasing the inflow valves to this 27 mm size. It was difficult to conduct these tests using the ERDA blood pump housing. Therefore, the tests were performed with an 8 cm Kwan-Gett heart developed previously at the University of Utah. For this test the heart was driven at 100 beats/minute and 35% systole with a six psi drive pressure, a 100 mm Hg arterial pressure and no vacuum. Results of this test indicate that there is a difference of as much as 1 liter/minute between the 27 and 29 cm size valves at an inflow pressure of 20 mm Hg (Figure IX-3). It is believed that these tests can be extrapolated to the ERDA ventricle indicating that the use of a 29 mm size inflow valve is preferable.

Valve Orientation

Effects of the valve orientation on cardiac output were evaluated by conducting a series of tests which entailed rotating the inflow and outflow valve separately 90°

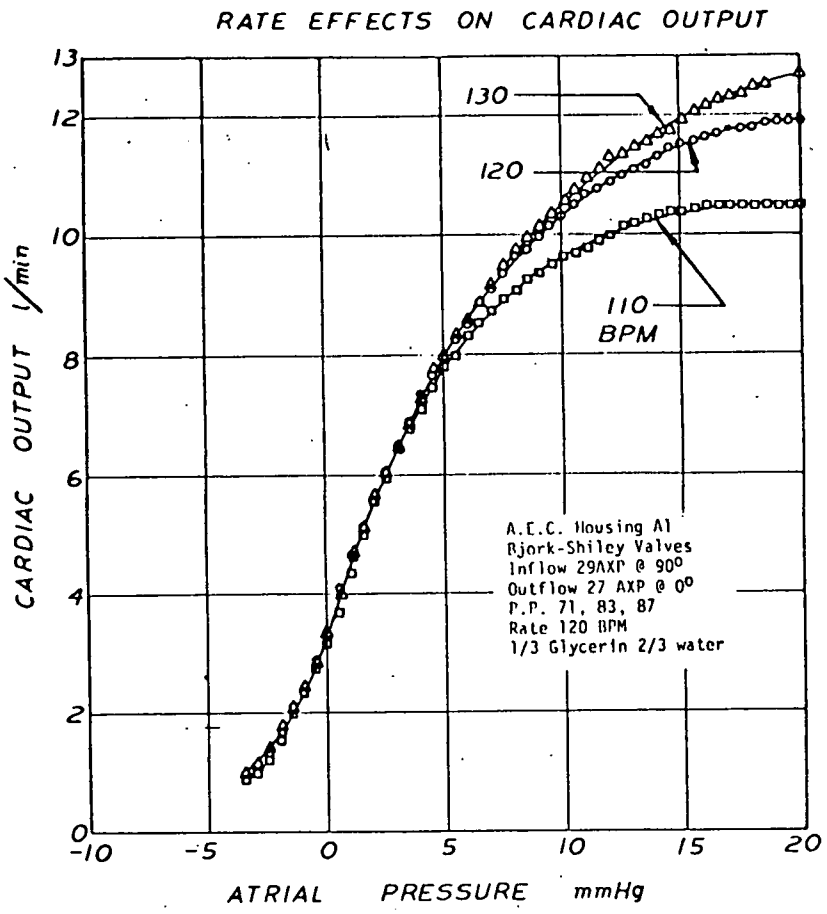


Figure IX-1 Cardiac function curve at several pumping rates.

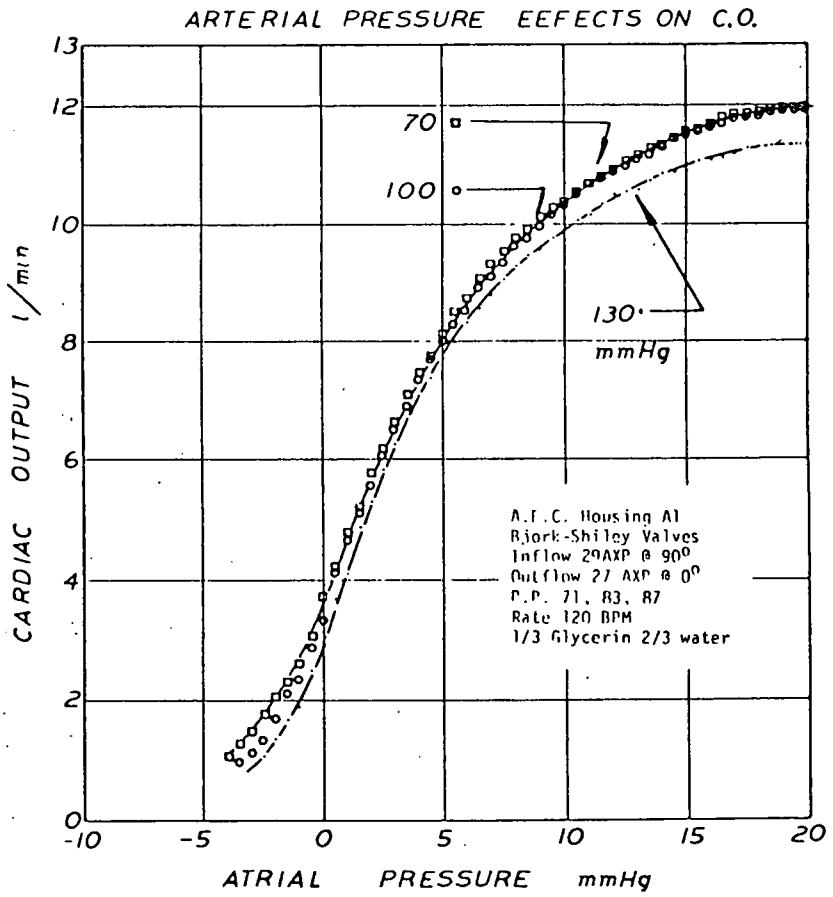


Figure IX-2 Cardiac function curve at several aortic pressures.

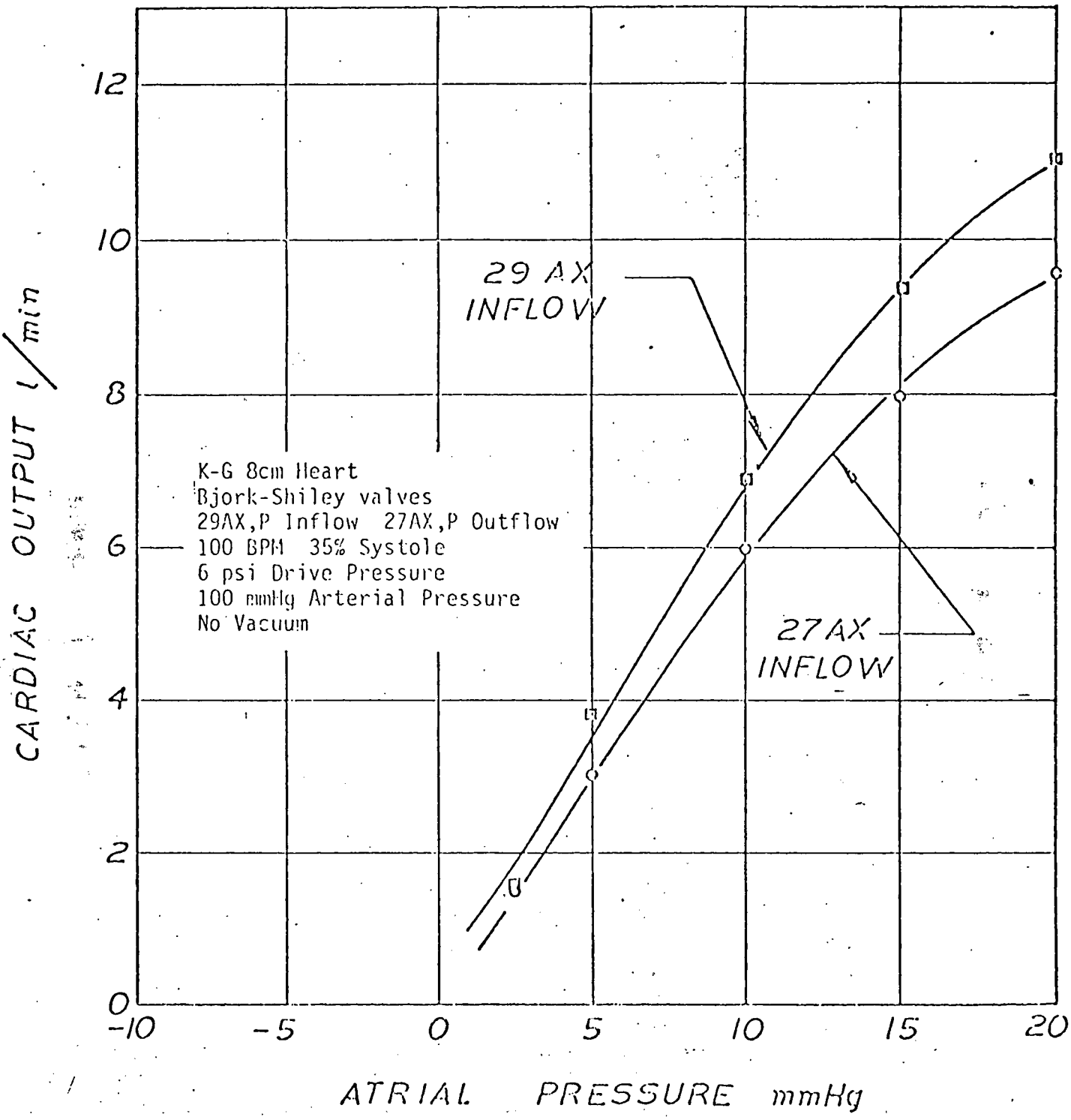


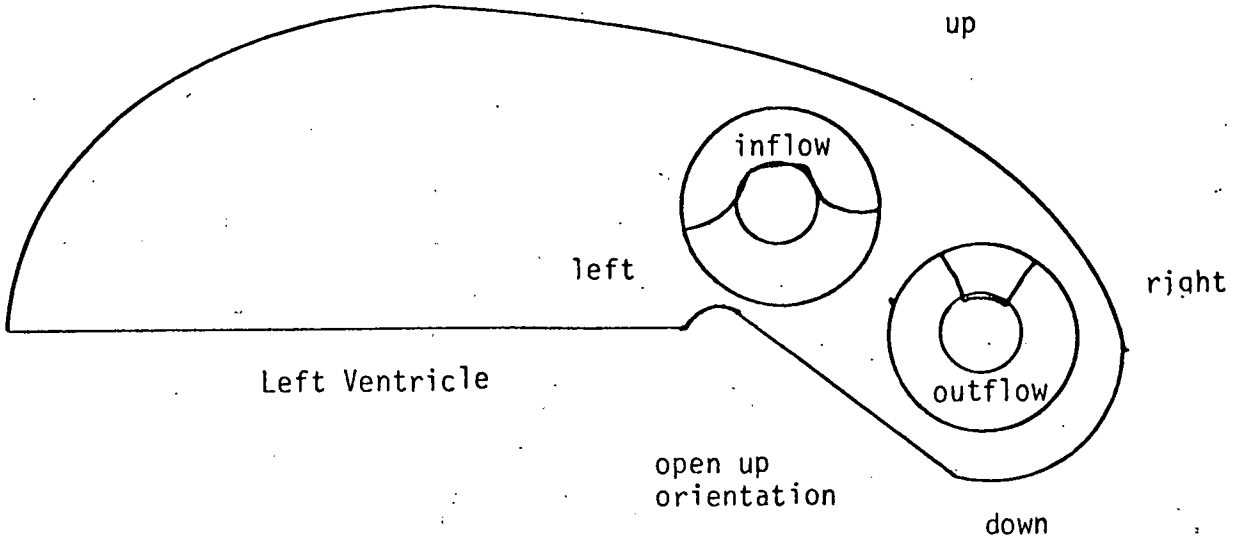
Figure IX-3: Comparison of Two Inflow Valve Sizes

at a time and repeating the function curve test. Changes in cardiac output and changes in the slope of the cardiac function curve were observed during these tests. However, for the ERDA left ventricle, these changes were small (See Figure IX-4).

Three tests were performed to determine the hemolysis rate of the ERDA ventricle. Procedure for this test is as follows: blood is drawn from the system as a 4 cm sample which is spun in the centrifuge for 30 minutes and the plasma removed. The plasma is then respun for about 10 minutes to remove any remaining red blood cells. The sample is analyzed with a spectrophotometer which scans between 0.600 and 0.516 microns. Calibration is performed to give the milligram percent of free plasma hemoglobin which is based on the optical density of the serum sample. Results of this test indicate that the hemolysis rate of the ERDA left ventricle is about one-third of the hemolysis rate of an 8 cm Kwan-Gett heart when pumped in what is considered a standard configuration mode, i.e. 6 psi drive pressure, 100 mm outflow pressure, at 100 beats/minute (See Table IX-1 for results).

Power Requirements

Power requirements and steady state pressures for the entire blood pump were determined using a Donovan mock circulation system. This system has four chambers, a systemic reservoir, a pulmonary-arterial reservoir, a pulmonary-venous reservoir and a systemic-arterial reservoir. Furthermore, the mock circulation includes both pulmonary and systemic resistances that closely duplicate resistances found in the natural circulation system. The pulmonary and systemic systems respond well to pressure changes and very closely duplicate the natural system. The compliance of the systemic venous chamber is 10 L/mm Hg. The compliance of the pulmonary arterial chamber is approximately 1 ml/mm Hg and the compliance of the pulmonary venous chamber is approximately 5 ml/mm Hg. This mock circulation system also has a built-in turbine-type electromagnetic flow meter. Results from testing the entire heart on the Donovan mock circulation system driven at a speed of 120 beats/minute, using water as the mock circulatory fluid, indicate that power requirements are close to design values. To conduct the test, the motor speed was held constant and controlled to remain constant in the right heart. Flow pressure was varied to include not only reasonable physiological values, but extremes both above and below these values. At this point in the evaluation testing, only steady state results were obtained. The mock circulation requires approximately 30 seconds to reach steady state when the right ventricular inflow pressure has been changed. All other pressures and flows are controlled and seek a level determined by the blood pump characteristics and the mock circulatory characteristics. If the pump under testing has very good characteristics, the pressures and flows will be physiologically reasonable. For the blood pump under testing, unreasonable right inflow and left inflow pressures were required for high pump flow rates. However, for flow rates of about 10 L/min and below, inflow and outflow pressures appeared to have acceptable levels. Measurements indicate that maximum efficiency occurs between 8.5 and 10.5 L/min, and is in the range of 55% overall efficiency. Power level requirements were slightly in excess of the design maximum of 6 watts for high flow rates. Power input during this test was measured at the motor end of the flexible drive shaft.



INFLOW VALVE

OUTFLOW VALVE	open up	open left	open down	open right
open up	11.1	--	11.3	11.3
open left	10.1	10.9	10.8	10.0
open down	11.0	11.1	11.9	11.0
open right	10.8	10.7	11.0	11.2

Figure IX-4: Changes in cardiac output with valve orientation.

TABLE IX-1

HEMOLYSIS DATA

Test	Rate BPM	Flow L/min	Hct. %	ΔHb mg%	Slope $\frac{mg\%}{min}$	H.I. $\frac{mg\%}{100\ L}$	H.I. Ratio
1	120	10.2	49	9.6	0.066	0.0072	0.30
2	120	10.2	43	5.1	0.043	0.0053	0.22
3	138	10.4	50	10.2	0.0943	0.010	0.42

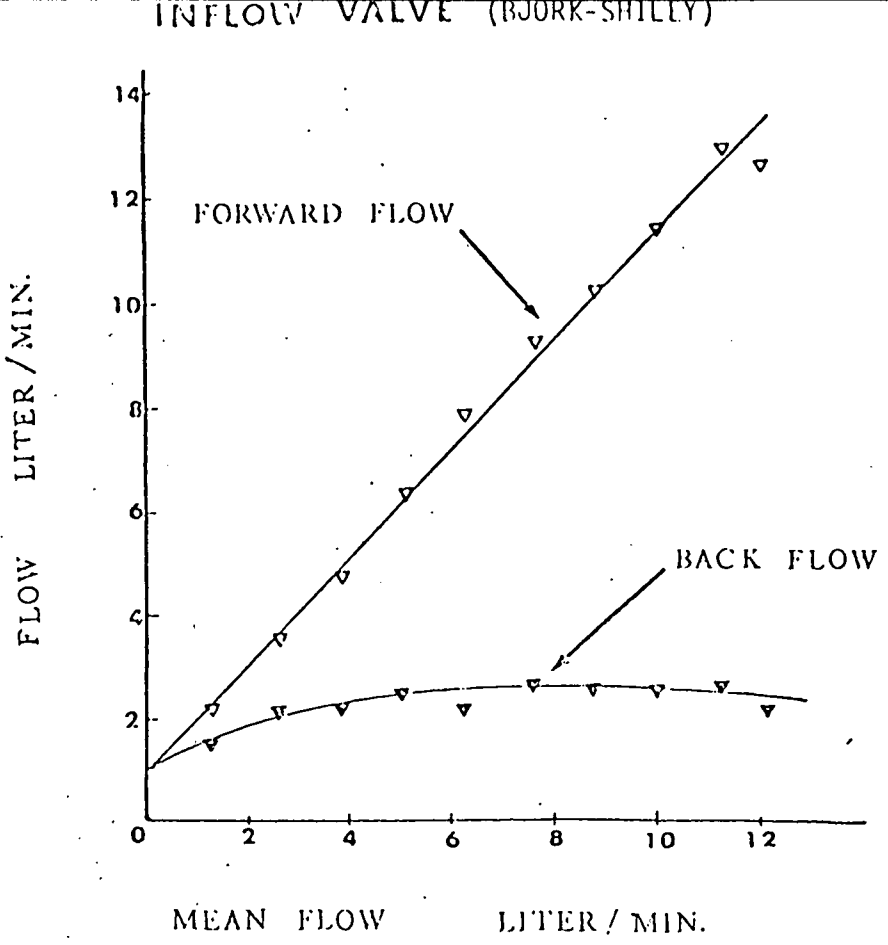
Valve Regurgitation

A mock circulation system was instrumented with a Biotronics electromagnetic flow meter, both on the inflow and outflow of the pump, to determine valve regurgitation. Traces of the flow wave form were recorded on a strip chart recorder, and graphically integrated to determine the forward flow and back flow through the valve over several cycles of pumping. Results of this test indicate there is a large amount of back-flow occurring with Bjork-Shiley valves, both in the inflow position and the outflow position, which amounts to approximately 2 L/min. See Figure IX-5 for data.

Another test was performed by replacing the outflow valve with a special valve designed by the General Motors Research Laboratory and the test was repeated. A significant drop in outflow valve regurgitation was noted. The reduction in regurgitation was approximately 0.5 L/min, which shows that considerable improvement in cardiac output is possible with careful valve selection or improved valve design. See Figure IX-6 for data.

Cardiac Output Estimation

A method was developed to estimate cardiac output of the AEC blood pump during in vivo tests. This method requires measuring either the aortic pressure or ventricular pressure of the left ventricle. From these pressure traces, a time duration for systole can be approximated. Since the ERDA blood pump operates under a variable systolic mode, the cardiac output can be correlated with this systolic time. Results of this test indicate that measuring the ventricular pressure is a better indication of cardiac output than measuring the aortic pressure systolic time interval. See Figure IX-7 for experimental data.



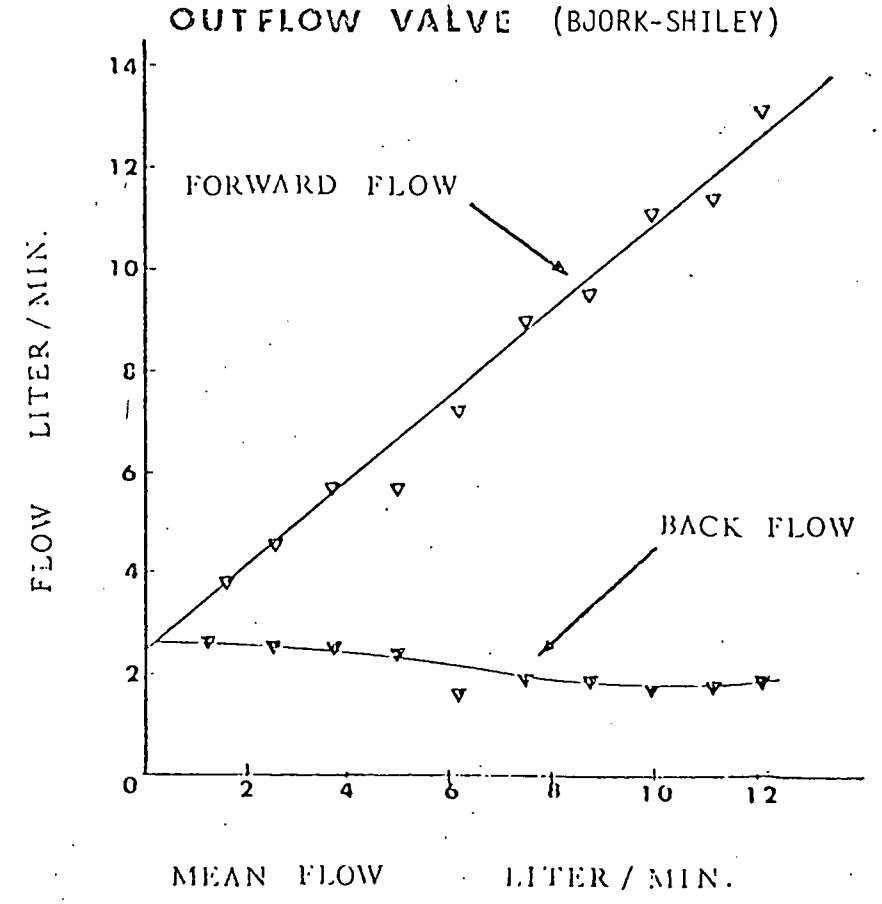
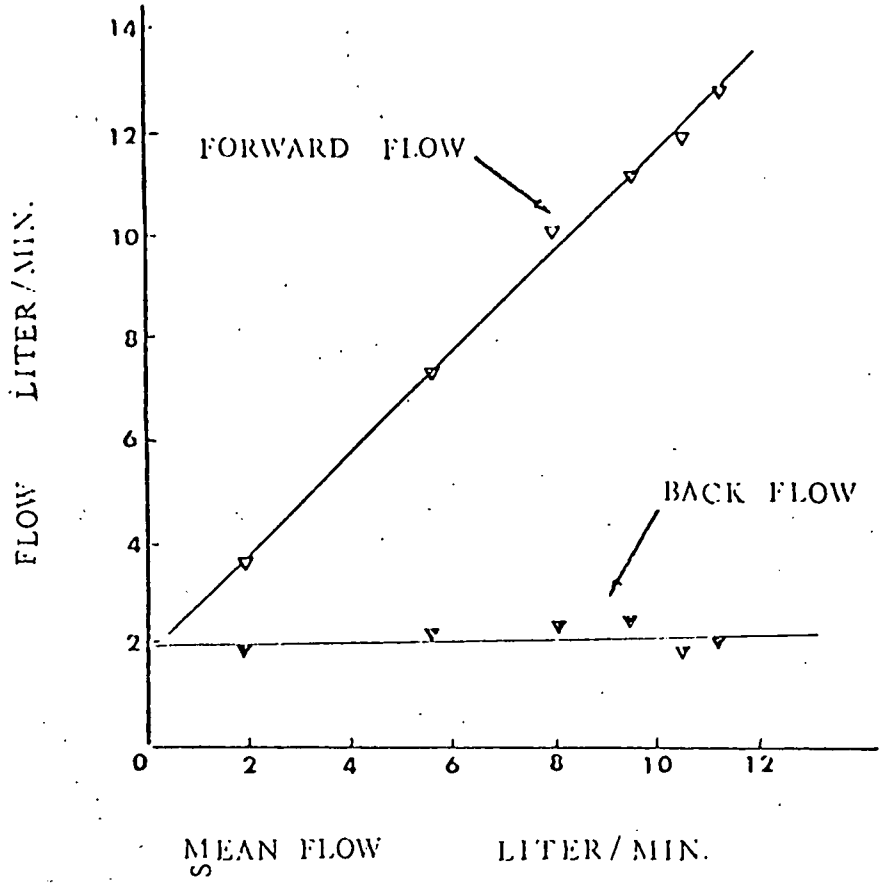


Figure IX-5: Valve regurgitation (2 Bjork-Shiley)



OUTFLOW VALVE (GENERAL MOTORS)

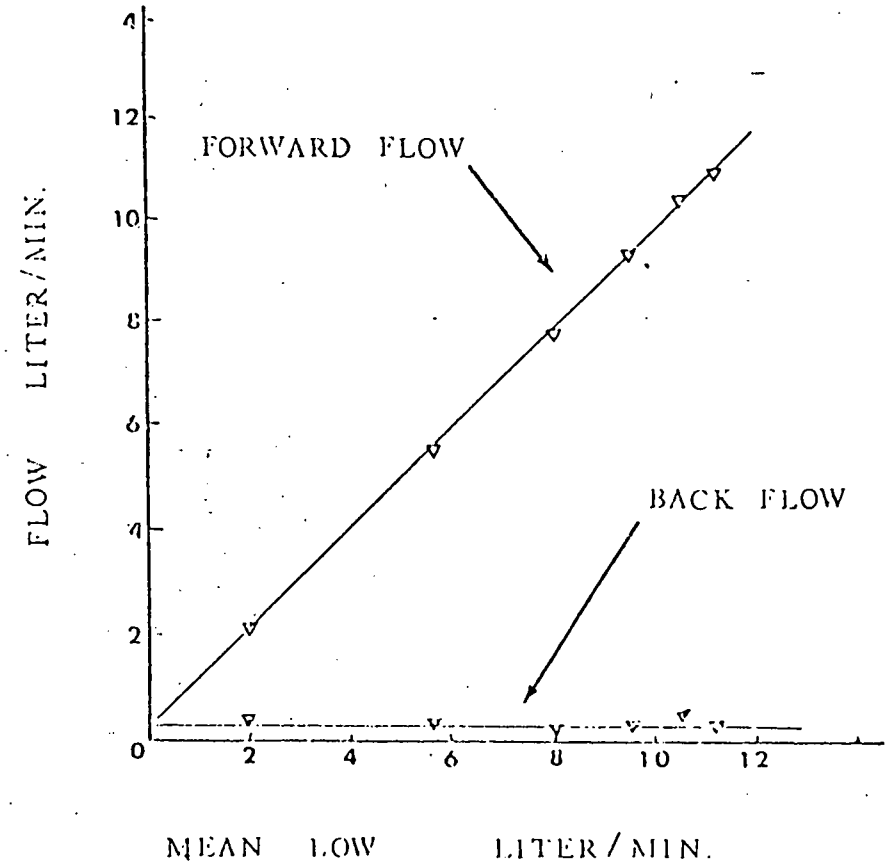
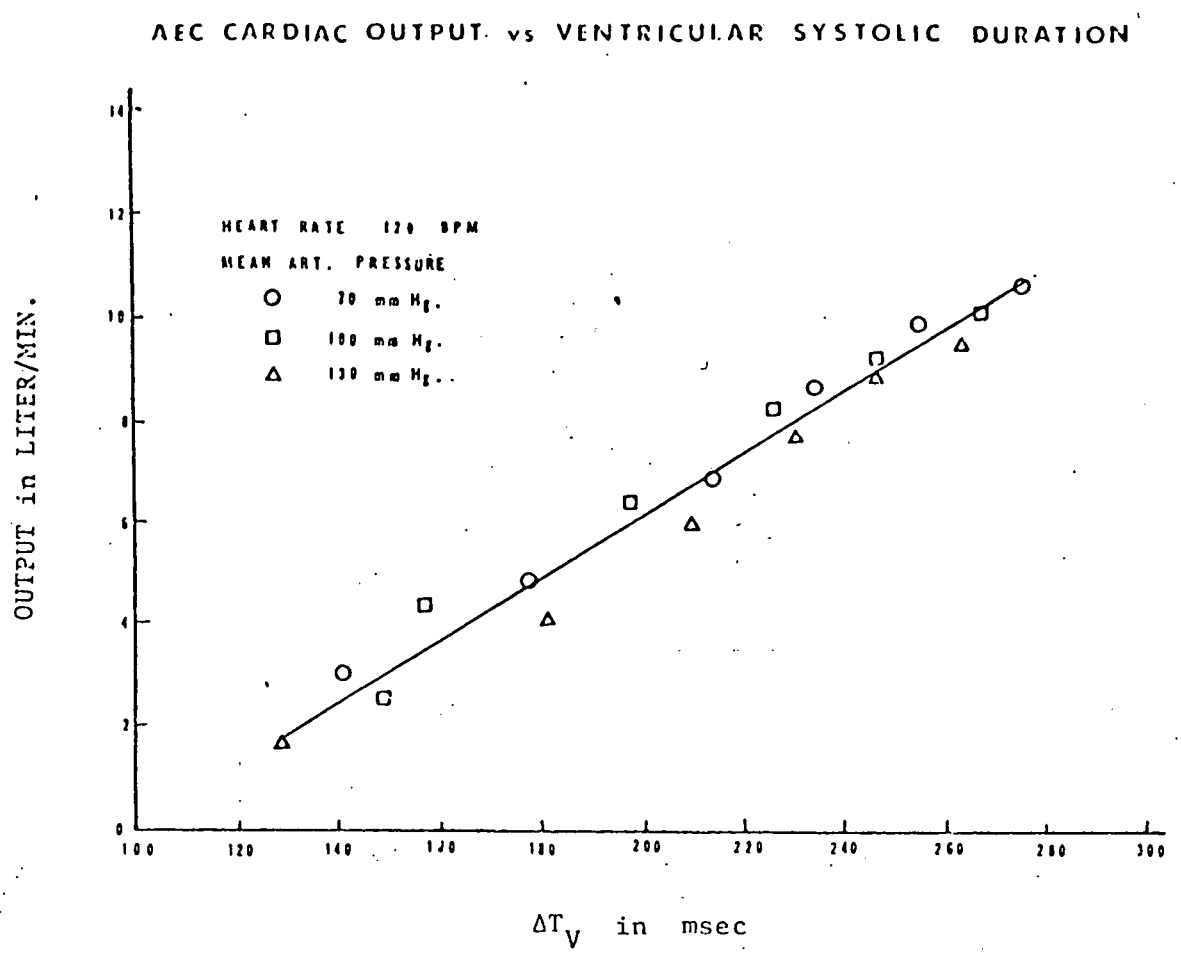


Figure IX-6: Valve regurgitation (Bjork-Shiley and General Motors)



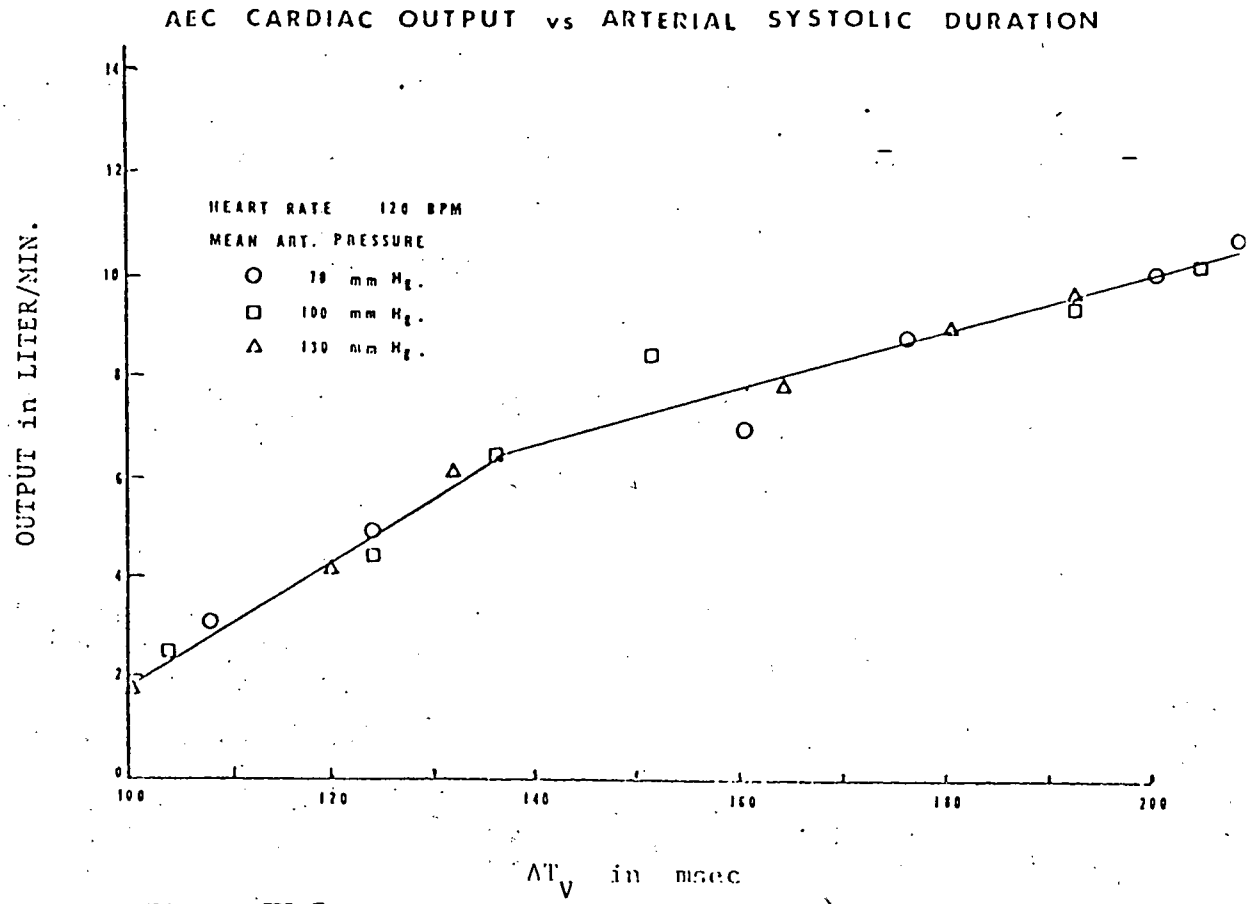


Figure IX-7: Cardiac output estimation.

X: IN VITRO STUDIES AND EXPERIMENTS

1. Mock Circulation Studies

Calibration of Instruments

The systemic flow meter in the mock circulatory system built by Westinghouse Astronuclear Laboratory was calibrated by using a roller-pump to pump a 33% glycerin in water solution into the systemic arterial chamber, through the systemic flow meter and into the systemic venous chamber. The actual flow rate was calculated by determining the time required to pump 19 liters through the flow meter. The pulmonary flow meter was calibrated by comparison with the systemic flow meter. The systemic and pulmonary flow calibration curves are shown in Figure X-1. The motor speed control was calibrated for torque under a static load. The torque meter calibration curve is shown in Figure X-2. The pressure gauges on the mock circulatory system were calibrated against a mercury manometer and found to have no observable error over the range of the instruments.

Pressure and Volume Measuring Systems

A strain gauge pressure transducer was used to measure ventricular pressure. The analog computer circuit used to produce a pressure signal from this transducer is shown in Figure X-3. In order to determine the instantaneous fluid volume in the left and right ventricles respectively, the system shown in Figure X-4 was used. In this arrangement the pump was connected to the mock circulatory system so that the left ventricle receives fluid from the systemic venous chamber and pumps into the systemic arterial chamber while the right ventricle receives fluid from the pulmonary venous chamber and pumps back into the pulmonary arterial chamber. The circulations of the left and right ventricles were closed systems so that any change in volume of fluid in the ventricle caused a corresponding change in the volume of air in the compliance chambers. This change in air volume caused a change in air pressure which is sensed by the pressure transducers on top of the chambers. The electrical circuit shown in Figure X-5 was used to convert the pressure transducer signals into a systemic volume signal. The electrical circuit shown in Figure X-6 was used to convert the pressure transducer signal from the pulmonary circulation into a pulmonary ventricular volume signal.

The pressure measuring system was calibrated against a mercury manometer and the volume measuring systems were initially calibrated by injecting 50 ml of fluid into the system and noting the resulting oscilloscope deflection.

Experimental Procedure and Results

All of the experiments were run using a mixture of 33% glycerin in water to simulate the viscosity of blood. Eight runs were made with the ventricles connected to the mock circulatory system as shown in Figure X-4. Pressure volume diagrams were generated by connecting the ventricular pressure signal to the horizontal axis of an oscilloscope

and the volume signal to the vertical axis of the oscilloscope and then photographing the resulting oscilloscope trace. During each run measurements were made of systemic ventricular output, pulmonary ventricular output, drive motor torque, systemic venous pressure, systemic arterial pressure, pulmonary venous pressure and pulmonary arterial pressure. All of the runs were made at a heart rate of 120 beats per minute. These data were used to calculate indicator power (which is the power delivered by diaphram to the blood in the ventricle), blood power (which is the energy delivered to the arterial blood relative to the venous blood), indicator efficiency and volumetric efficiency for each ventricle using Equation 1,2,3, and 4.

The indicator power is given by:

$$IP = K \times A \qquad (1)$$

where:

IP is indicator power in watts

A is area of pressure-volume diagram in cm^2

K is a volume and pressure scale and conversion factor which includes heart rate. K = 0.1144 watt/cm^2 for the left ventricle and 0.1565 watt/cm^2 for the right ventricle.

The power delivered to the blood:

$$BP = \frac{Q \times (Pa - Pv)}{450} \qquad (2)$$

where:

BP is blood power in watt

Q is ventricular output in L/min

Pa is mean arterial perssure in mm Hg

Pv is mean venous pressure in mm Hg

The indicator efficiency is given by:

$$IE = \frac{BP}{IP} \times 100 \qquad (3)$$

where:

IE is indicator efficiency in %

and the volumetric efficiency

$$VE = \frac{Q \times 100}{120 \times IV} \quad (4)$$

where:

VE is volumetric efficiency in %

IV is indicator stroke volume measured from the pressure-volume diagrams in liters.

The results of these calculations for the left ventricle are shown in Table X-1 and for the right ventricle in Table X-2. Shaft power, which is the output power of the electric drive motor was calculated for each run using Equation 7.

$$SP = 0.66554 \times T \quad (5)$$

where:

SP is shaft power in watt

T is drive motor torque in in-oz

Note that Equation 5 is correct only for a shaft speed of 900 rpm

The results given in Table X-1 and X-2 were combined to calculate a total heart indicator power and a total heart blood power using Euqations 6 and 7.

$$IP_T = IP_L + IP_R \quad (6)$$

where:

IP_T is total heart indicator power in watt

IP_L is left ventricle indicator power in watt

IP_R is right ventricle indicator power in watt

The power delivered to the blood is

$$BP_T = BP_L + BP_R \quad (7)$$

where:

BP_T is total heart blood power in watt

BP_L is left ventricle blood power in watt

BP_R is right ventricle blood power watt

The total heart shaft efficiency, total heart indicator efficiency and total heart mechanical efficiency were calculated using Equations 8, 9 and 10.

$$SE_T = \frac{BP_T}{SP} \times 100 \qquad (8)$$

SE_T is total heart shaft efficiency in %

$$IE_T = \frac{BP_T}{IP_T} \times 100 \qquad (9)$$

IE_T is total heart indicator efficiency in %

$$ME_T = \frac{IP_T}{SP} \times 100 \qquad (10)$$

ME_T is total heart mechanical efficiency in %

The results of these calculations are given in Table X-3. Note that the results in Table X-3 represent a composite of the ventricles run as independent pumps with the systemic arterial pressure held constant at a 100 mm of mercury and a pulmonary arterial pressure held constant at 15 mm of mercury.

A second set of experimental data were collected with the ventricles connected to the mock circulatory system in the normal fashion as a total artificial heart. During these runs measurements were made of cardiac output, drive motor torque, systemic venous pressure, systemic arterial pressure, pulmonary venous pressure and pulmonary arterial pressure. All of the runs were made with the heart operating at 120 beats per minute. The mock circulatory system was adjusted so that with a cardiac output of 6 liters per minute the systemic arterial pressure was regulated to 100 mm of mercury and the pulmonary arterial pressure was regulated to 15 mm of mercury. Once the mock circulatory system was adjusted it then controlled the arterial resistencies automatically. These data were used to calculate a shaft power, blood power and shaft efficiency for each run as before. The results of these calculations are shown in Table X-4.

Discussion

The volumetric efficiency and indicator efficiency of the left and right ventricles are shown as functions of cardiac output in Figure X-7. It is obvious from these curves that at 10 liters per minute output, only 75% of the blood entering the left ventricle is being pumped out into the systemic arteries and about 62% of the blood entering the right ventricle is pumped out into the pulmonary artery. This indicates that about 25% of the cardiac output is being lost because of valve leakage. The volumetric efficiency is contributing heavily to the low indicator efficiencies of both the left and right ventricles.

The shaft power required to drive the total artificial heart and the corresponding shaft efficiency of the total artificial heart are shown in Figure X-8 which is plotted from data in Table X-4. It should be noted that the systemic and pulmonary resistances were

being regulated automatically by the mock circulatory system during the runs plotted in Figure X-8. The maximum shaft efficiency of the total heart is 40% at cardiac output of 10 liters per minute; this low efficiency is due in large part to the low volumetric efficiency of the ventricles, which in turn is caused by valve leakage. If the volumetric efficiency of both ventricles could be increased to 100%, that is if valves which have no leakage could be used, then the shaft efficiency of the heart would increase to an estimated value of 50%. The remaining power losses in the heart seemed to be related to pressure drops through the outflow valves. For example, consider the typical pressure-volume diagram of the left ventricle shown in Figure X-9. Note that after the inflow valve closed the pressure increased at practically constant volume until the ventricular pressure reached about 145 mm Hg, at which point the outflow valve appeared to open and the ventricle began emptying with a gradual decrease in ventricular pressure. The arterial pressure at the instance of opening the outflow valve should be on the order of 75 or 80 mm Hg, since the mean arterial pressure was about 100 mm Hg. The existence of this high pressure in the ventricle before emptying began represented a sizeable energy loss. The energy did not appear in the arterial blood. This high ventricular pressure may be caused by outflow valve resistance, or it may be caused by some inertial effects within the ventricle.

Figure X-10 shows the overall performance of the total heart with systemic and pulmonary resistance being regulated by the mock circulatory system. Note that as the cardiac output goes above about 7 liters per minute the pulmonary venous pressure begins to increase rapidly and there is a corresponding rapid increase in pulmonary artery pressure even though the pulmonary resistance is being decreased by the mock circulatory system. These are symptoms of left ventricular failure and can be expected to occur in the calf if cardiac outputs of greater than 7 or 8 liters per minute are required.

Figure X-11 shows a typical ventricular pressure and ventricular volume trace as a function of time with the ventricle pumping 6.7 liters per minute at a mean arterial pressure of 100 mm Hg. Note once again that during the early stages of systole the ventricular pressure is much greater than the arterial pressure at that time. It is obvious from the ventricular volume trace that the duration systole is less than the duration of diastole. For purposes of comparison Figure X-12 shows a ventricular volume trace with the ventricle pumping 10.3 liters per minute at a mean arterial pressure of 100 mm Hg. The diastolic and systolic times in this trace are approximately the same. This illustrates the capability of the AEC Blood Pump to increase it's diastolic time with decreasing cardiac outputs. Figure X-13 shows a photograph of the overall system used to obtain the results given here.

Error Analysis of Blood Power Calculations

The equation used to calculate blood power, Equation 2, is correct only for steady flow and is an approximation for pulsatile flow. This equation is used because it is simple to obtain a mean pressure and a mean flow. The alternative would be to have a rather complicated system of measuring instantaneous flow. In order to determine the magnitude of error involved in using this equation an analysis was made for the worst possible case in which output from the ventricle is zero during diastole and constant during systole. This condition is roughly approximated by the AEC Blood Pump at high

flow rates. For normal arterial resistance and compliance with a cardiac output of 10 liters per minute the error in Equation 2, as applied to the left ventricle, is -2.32% which means that the power calculated by Equation 2 is 2.32% less than the actual power being delivered at the arterial blood relative to the venous blood. The error in Equation 2 as applied to the right ventricle is -25.2% which means that the calculated power is 25.2% less than the actual power being delivered by the right ventricle to pulmonary arterial blood. This fact may account in part for the low efficiencies calculated for the right ventricle. The blood power calculation for the total heart with a cardiac output of 10 liters per minute, a mean systemic arterial pressure of 100 mm Hg, a mean pulmonary arterial pressure 15 mm Hg, and Systemic and venous pressures 0 mm Hg, is in error by -5.5% for the conditions used in this error analysis. Since the worst condition was selected for this error analysis it is believed that the maximum error involved in the total heart blood power calculation using Equation 2 is less than 5.5% and does not warrant the use of a more complicated system which may actually increase the error because of increased complexity.

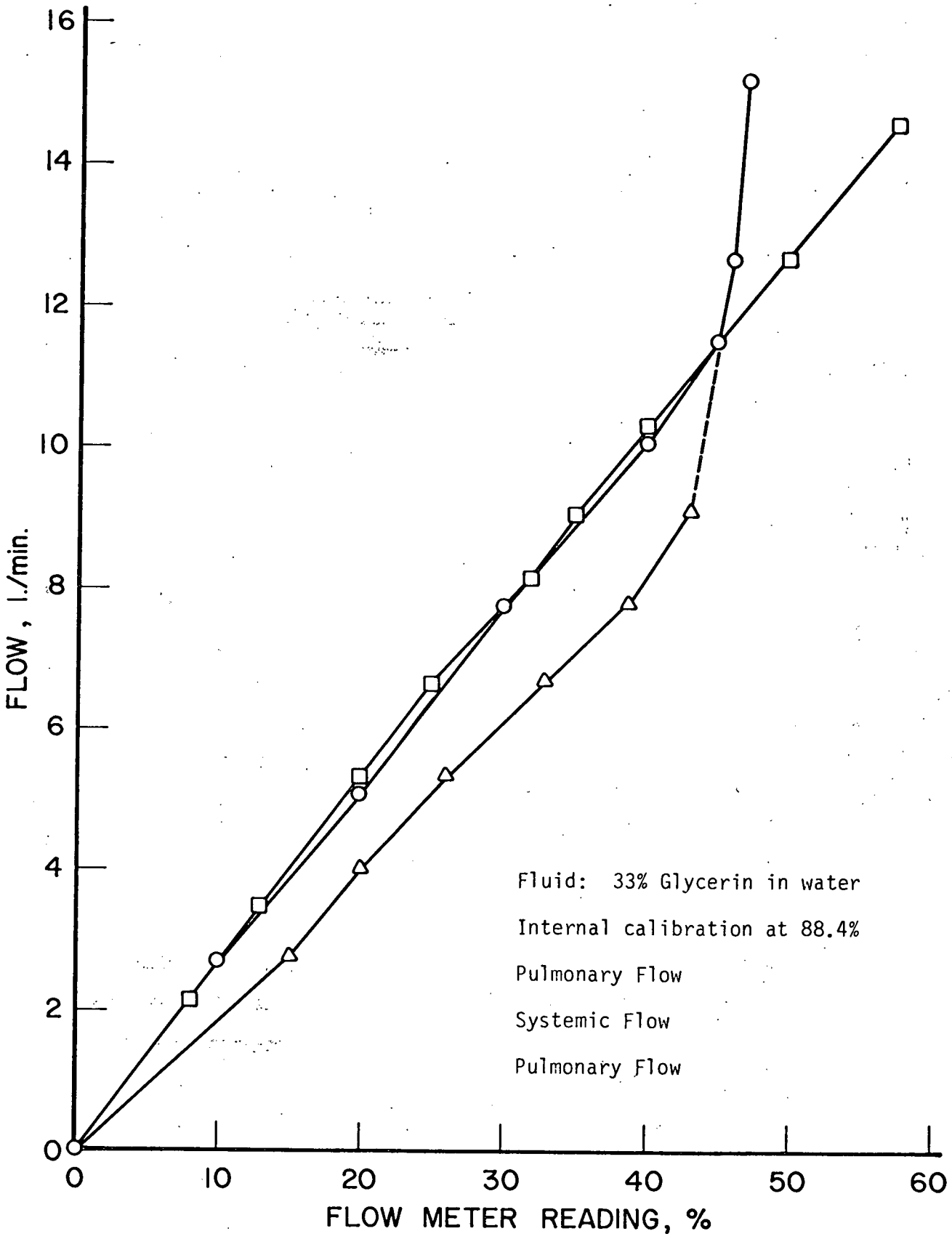


FIGURE X-1 : Flow meter calibration using Donovan mock circulation built by Westinghouse Astronuclear Laboratory

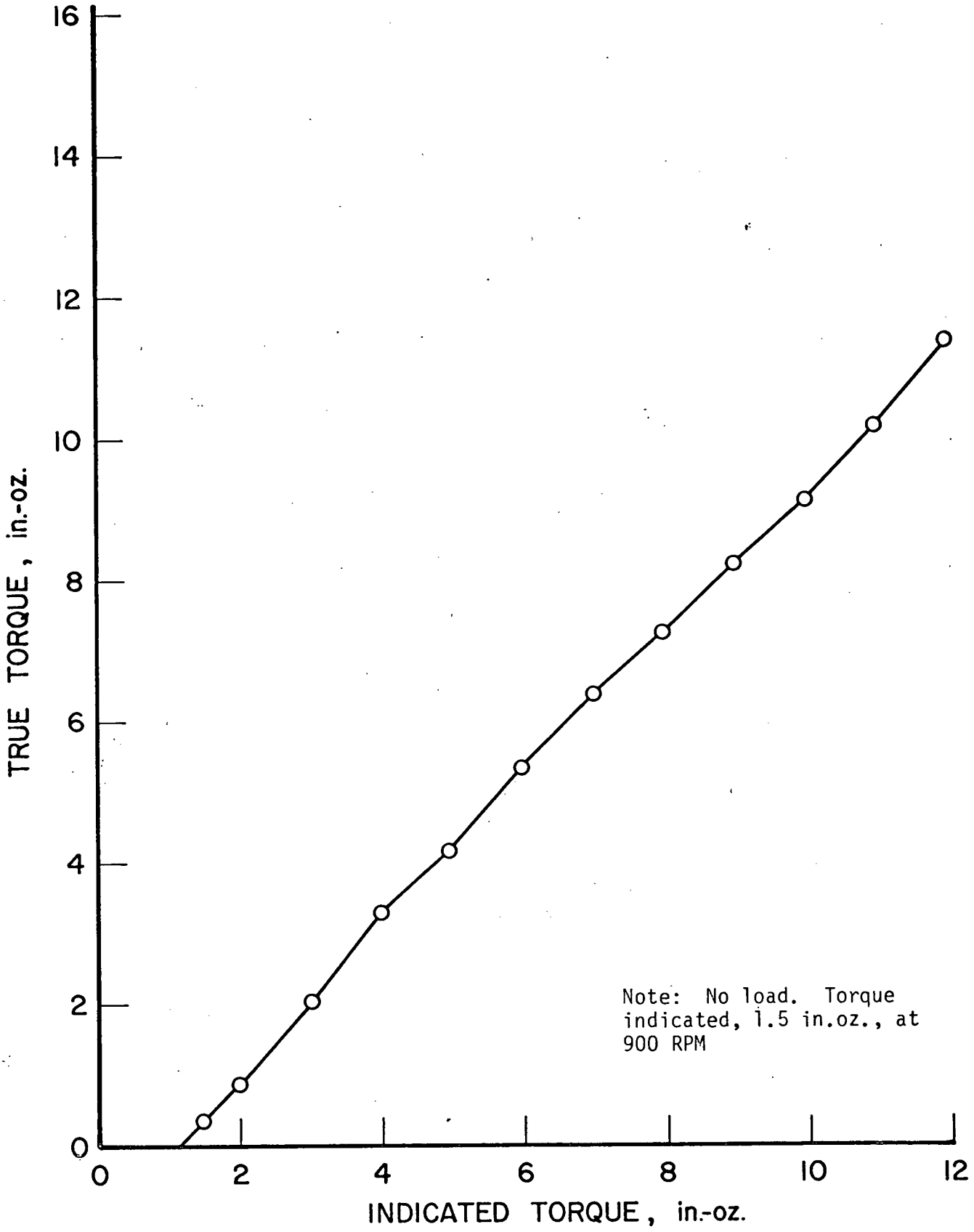


FIGURE X-2. Calibration of Motormatic Speed Control Number 9022.001.4 with Implantable Motor Under Static Load.

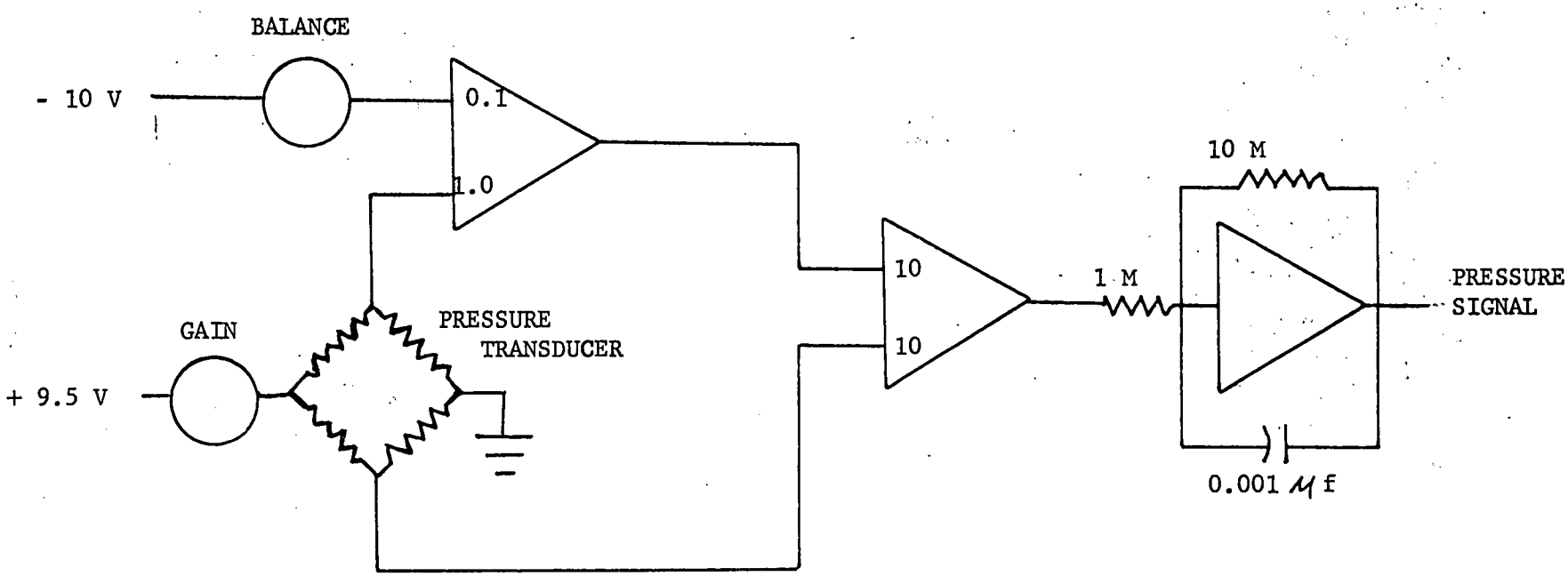
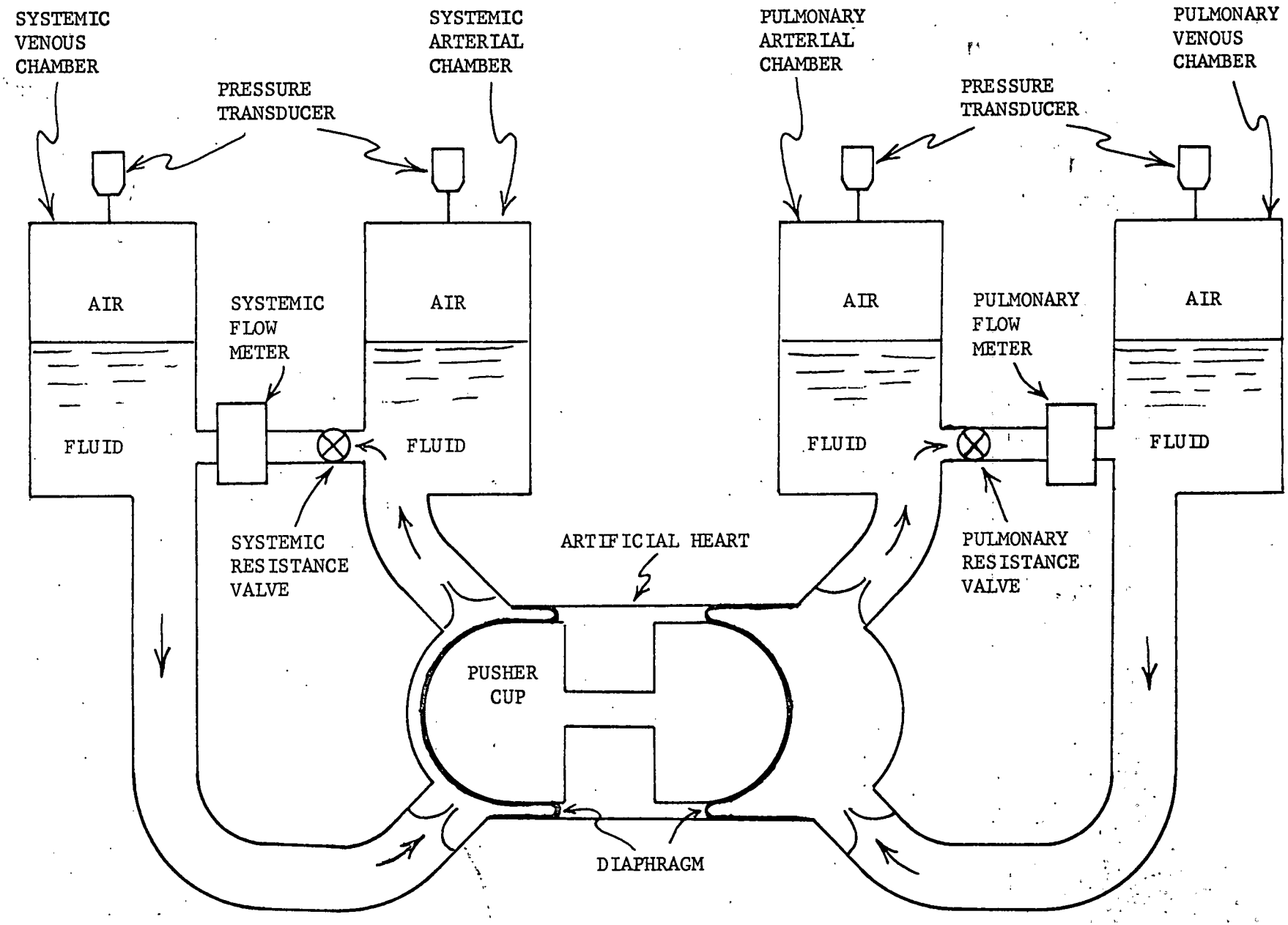


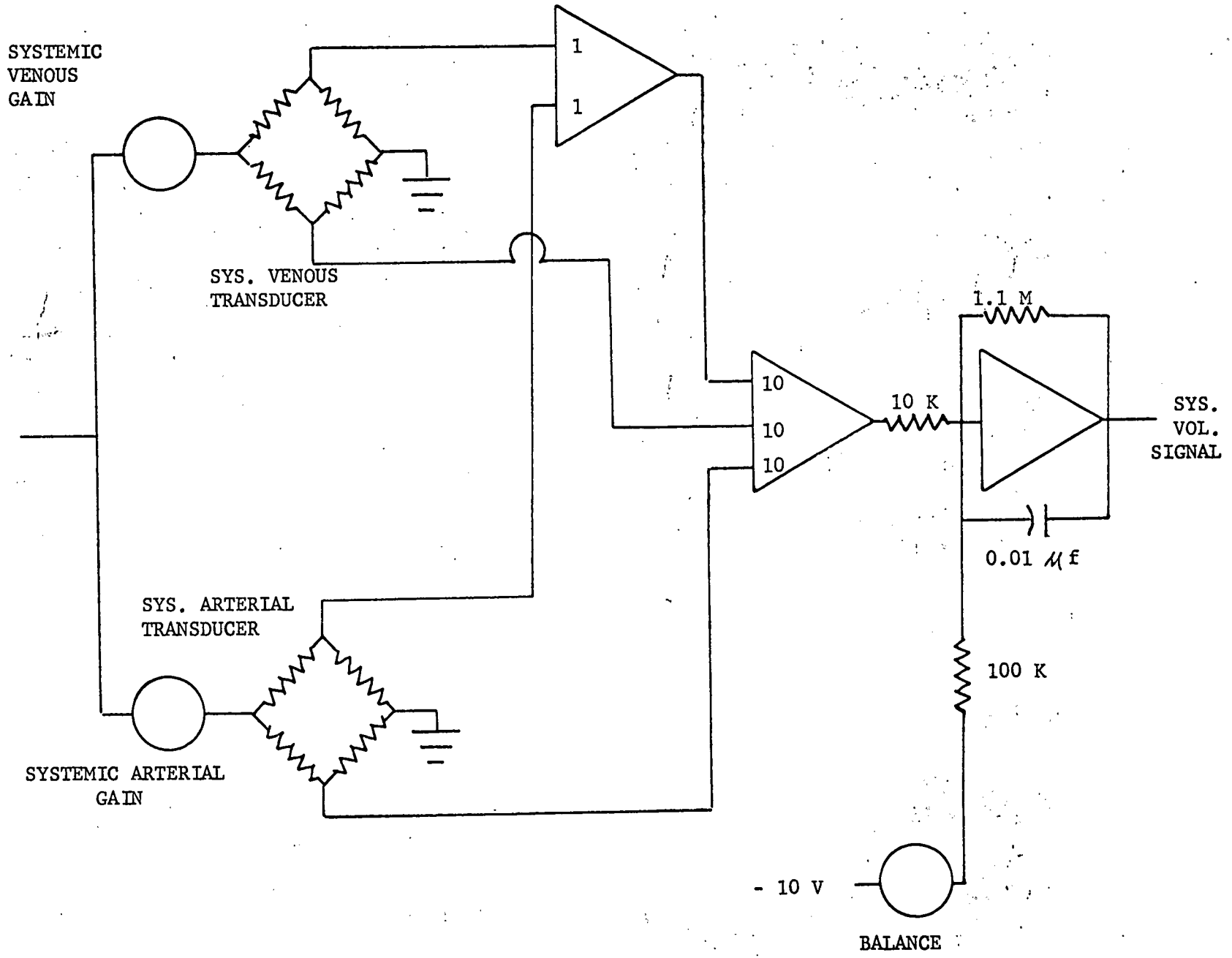
FIGURE X-3:

VENTRICULAR PRESSURE CIRCUIT



SCHEMATIC OF VENTRICULAR VOLUME MEASURING SYSTEM

FIGURE X-4:



SYSTEMIC VOLUME CIRCUIT

FIGURE X-5:

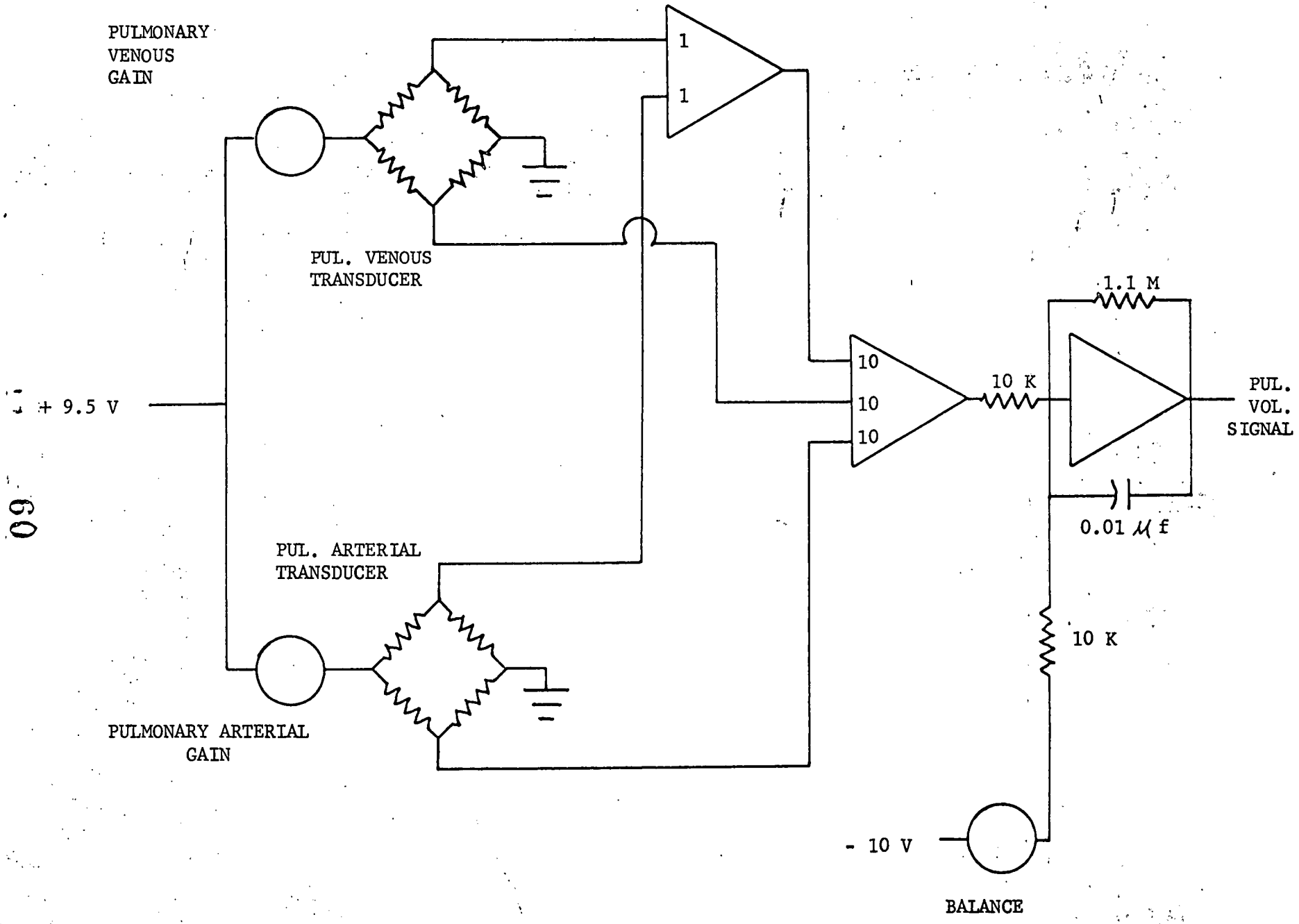


FIGURE X-6:

PULMONARY VOLUME CIRCUIT

TABLE X-1:

POWER AND EFFICIENCY RESULTS -LEFT VENTRICILE

RUN	VENOUS PRESS (mm Hg)	ARTERIAL PRESS (mm Hg)	VENTRICULAR OUTPUT (l/min)	INDICATOR POWER (watt)	BLOOD POWER (watt)	INDICATOR EFFICIENCY (%)	VOLUMETRIC EFFICIENCY (%)
A	-10.0	100	2.7	1.49	0.66	44	50
B	- 7.5	100	4.0	1.88	0.96	51	55
C	- 4.0	100	5.3	2.39	1.22	51	63
D	- 1.0	100	6.6	2.78	1.48	53	64
E	+ 1.5	100	7.7	3.18	1.69	53	68
F	+ 5.0	100	9.0	3.51	1.90	54	69
G	+ 9.5	100	9.7	3.70	1.95	53	71
H	+21.0	100	10.3	3.51	1.81	52	76

TABLE X-2:

POWER AND EFFICIENCY RESULTS -RIGHT VENTRICLE

RUN	VENOUS PRESS. (mm Hg)	ARTERIAL PRESS. (mm Hg)	VENTRICULAR OUTPUT (1/min)	INDICATOR POWER (watt)	BLOOD POWER (watt)	INDICATOR EFFICIENCY (%)	VOLUMETRIC EFFICIENCY (%)
A	-12.0	15	1.8	0.45	0.11	24	32
B	- 9.0	15	2.7	0.65	0.14	22	37
C	- 7.0	15	4.0	0.69	0.20	29	53
D	- 2.0	15	5.0	0.96	0.19	20	53
E	+ 1.0	15	6.0	1.05	0.21	20	56
F	+ 5.5	15	7.1	1.12	0.15	13	59
G	+ 7.0	15	7.6	1.46	0.14	10	60
H	+ 9.0	15	8.1	1.22	0.11	9	60

TABLE X-3:

POWER AND EFFICIENCY RESULTS - TOTAL HEART *

RUN	SHAFT POWER (Watt)	INDICATOR POWER (Watt)	BLOOD POWER (Watt)	SHAFT EFFICIENCY (%)	INDICATOR EFFICIENCY (%)	MECHANICAL EFFICIENCY (%)
A	2.53	1.94	0.77	30	40	77
B	3.86	2.53	1.10	28	43	66
C	3.59	3.08	1.42	40	46	86
D	4.79	3.74	1.67	35	45	78
E	4.86	4.23	1.90	39	45	87
F	5.46	4.63	2.05	38	44	85
G	5.59	5.16	2.09	37	41	92
H	5.46	4.73	1.92	35	41	87

* This table is a composite of the left and right ventricle results with systemic arterial pressure fixed at 100 mm Hg and pulmonary arterial pressure fixed at 15 mm Hg.

TABLE X-4:

TOTAL HEART PERFORMANCE *

RUN	SYSTEMIC VENOUS PRESS. (mm Hg)	PULMONARY ARTERY PRESS. (mm Hg)	PULMONARY VENOUS PRESS. (mm Hg)	SYSTEMIC ARTERY PRESS. (mm Hg)	CARDIAC OUTPUT (L/min)	SHAFT POWER (Watt)	BLOOD POWER (Watt)	SHAFT EFFICIENCY (%)
I	-25	0	-10	82	1.4	1.73	0.36	21
J	-20	+2	-4	96	2.7	2.20	0.73	33
K	-12	+11	-3	99	4.0	3.53	1.11	31
L	- 7	17	-2	101	5.3	4.26	1.50	35
M	-3½	18	+3	105	6.7	4.79	1.84	38
N	-1½	20	+4½	107	7.8	5.46	1.78	33
O	+1½	24	+10	110	9.1	6.06	2.48	41
P	+4	37	+26	111	9.8	6.79	2.57	38

* Total heart connected to mock circulation correctly. Systemic arterial and pulmonary arterial pressures set at 100 and 15 mmHg respectively at 6 L/min cardiac output and automatically controlled by the mock circulation after that.

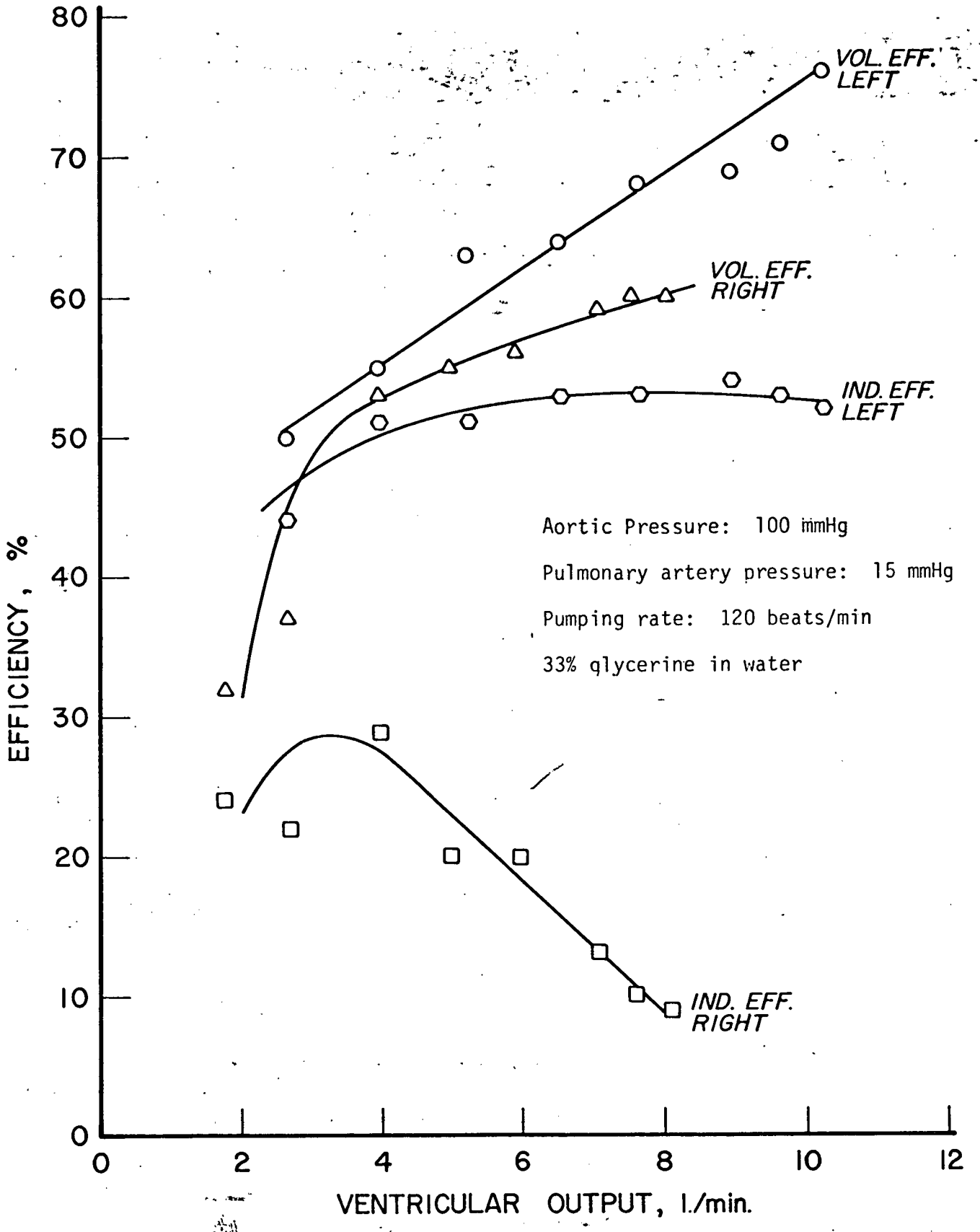


FIGURE X-7 : Efficiencies of AEC Bench Model Blood Pump Ventricles.

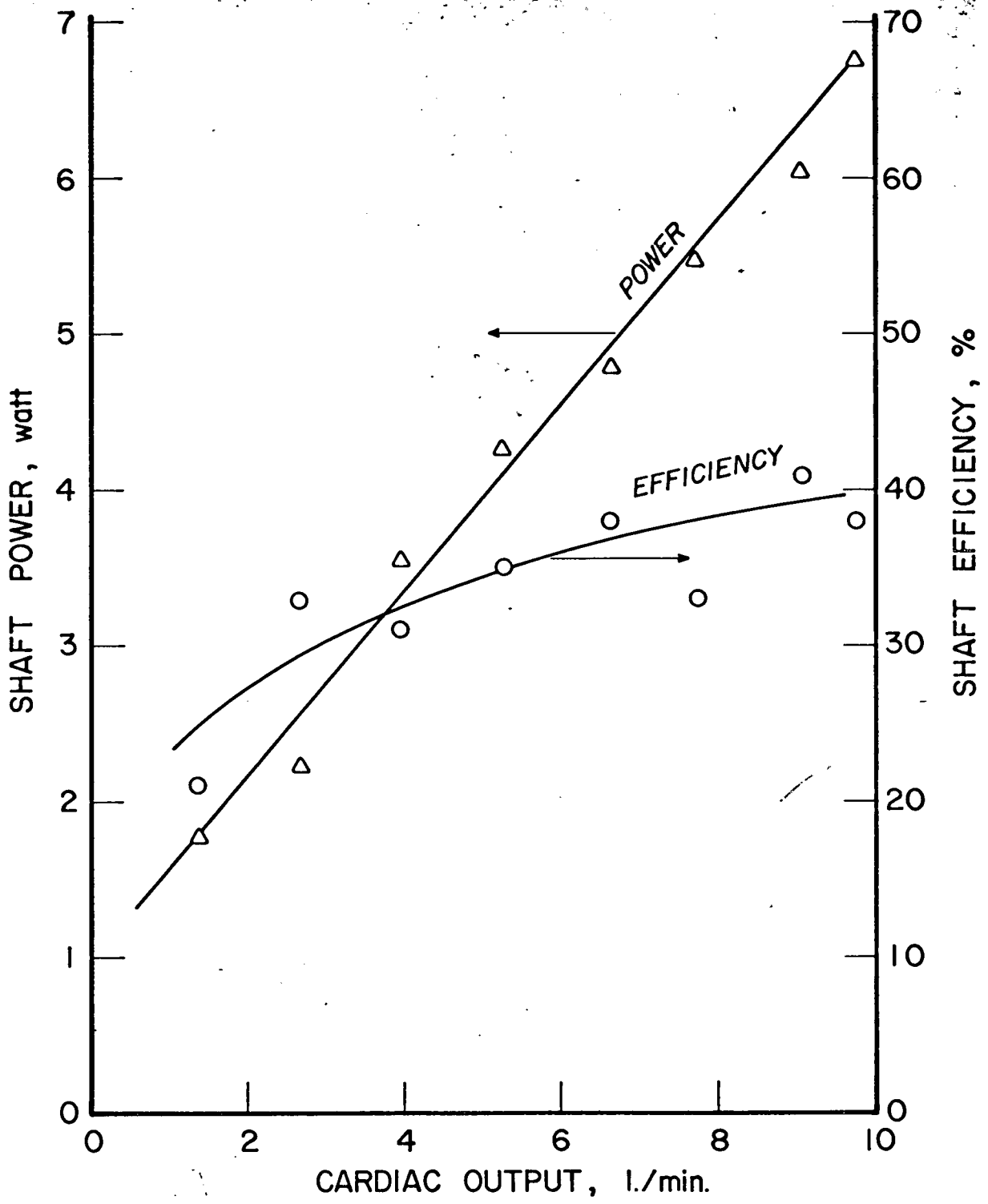
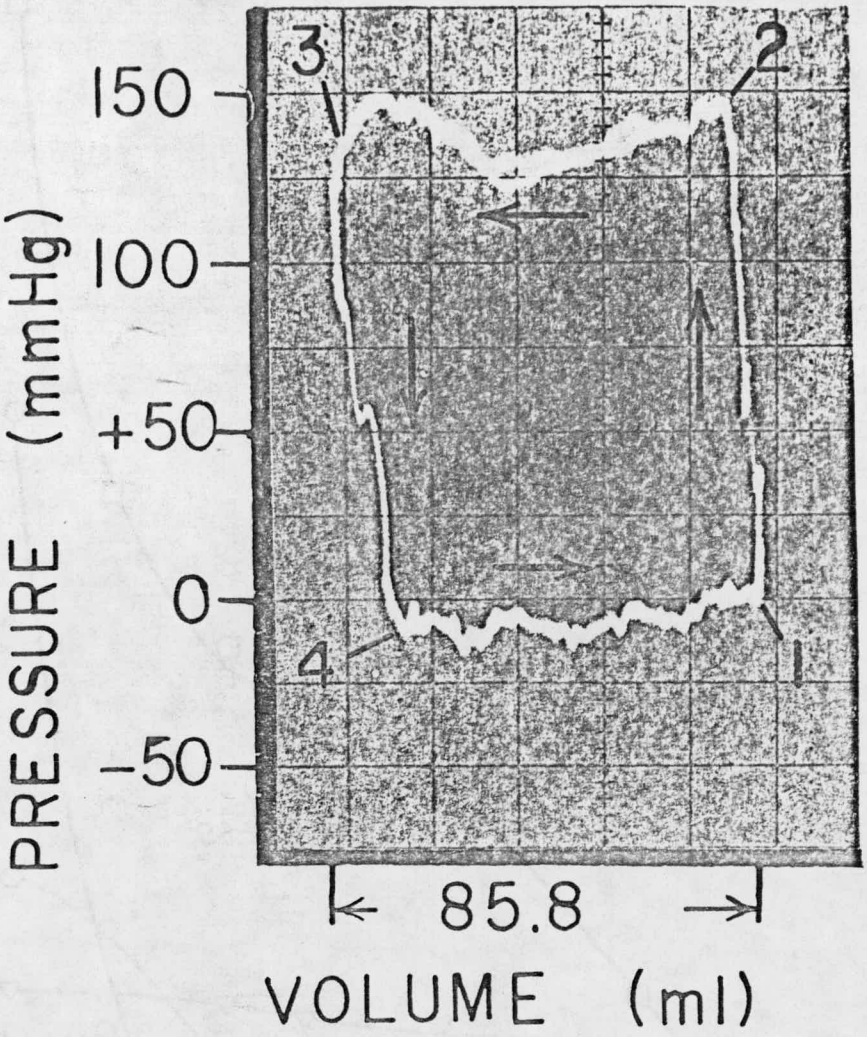


FIGURE X-8 : Overall power and efficiency of AEC Bench Model [illegible] Blood Pump

FIGURE X-9:



Pressure-volume diagram for left ventricle pumping 6.7 L/min with mean arterial pressure of 100 mm Hg.

Point 1 - Close inflow valve

Point 2 - Open outflow valve

Point 3 - Close outflow valve

Point 4 - Open inflow valve

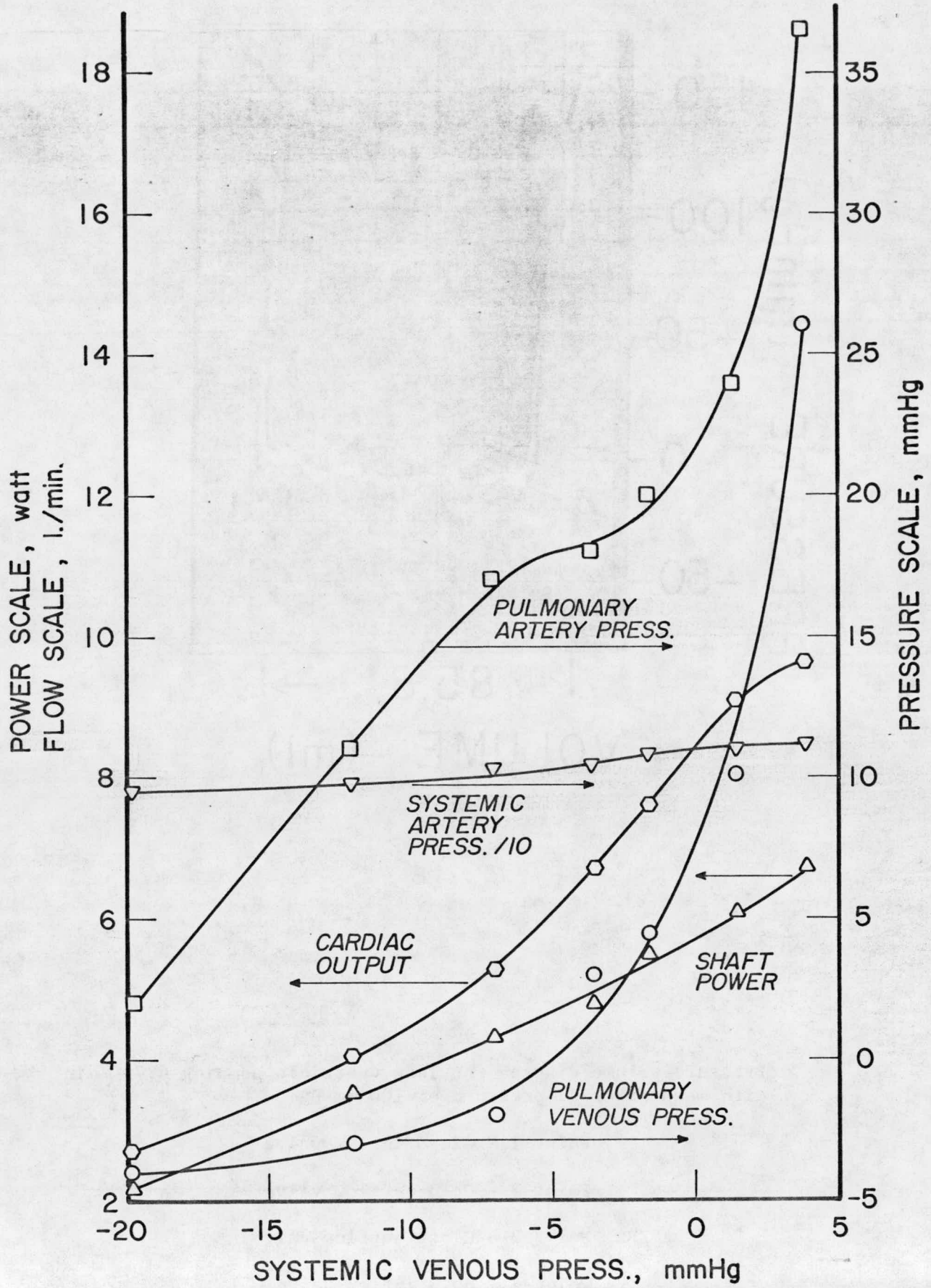
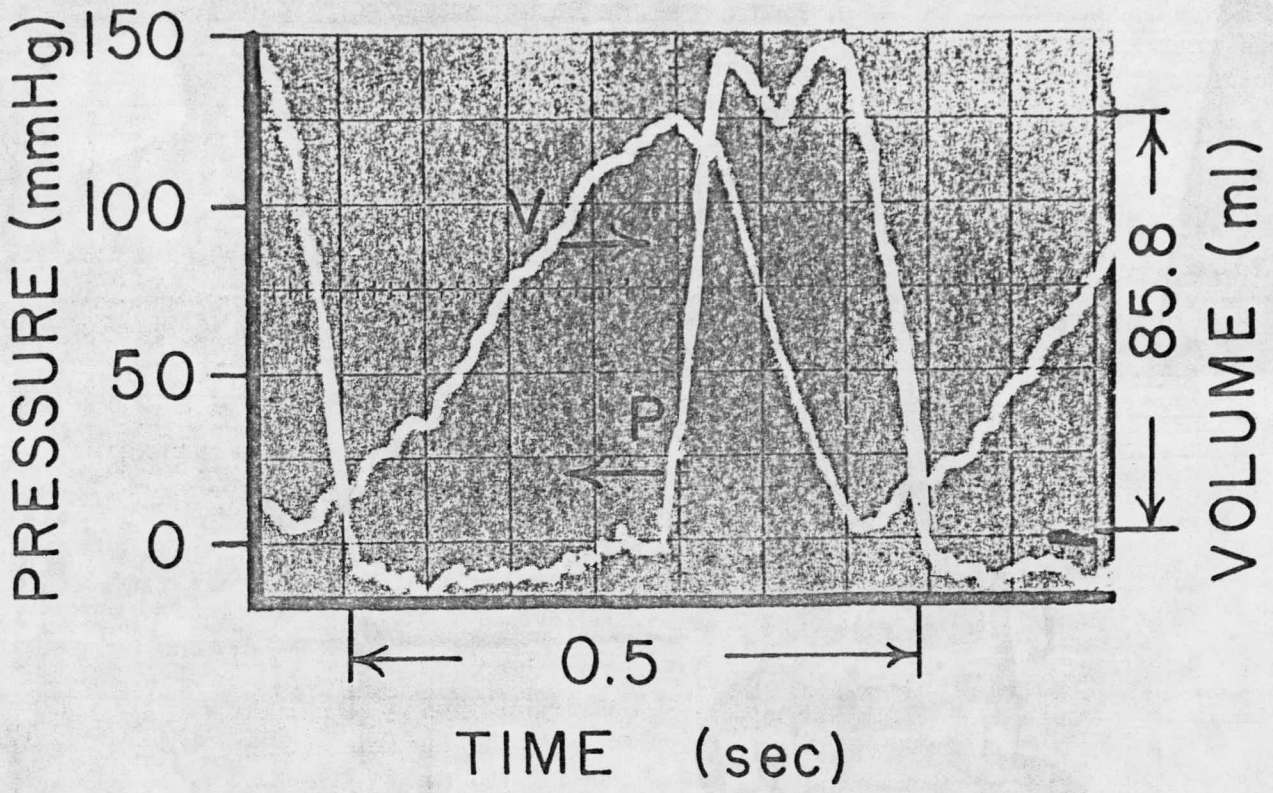


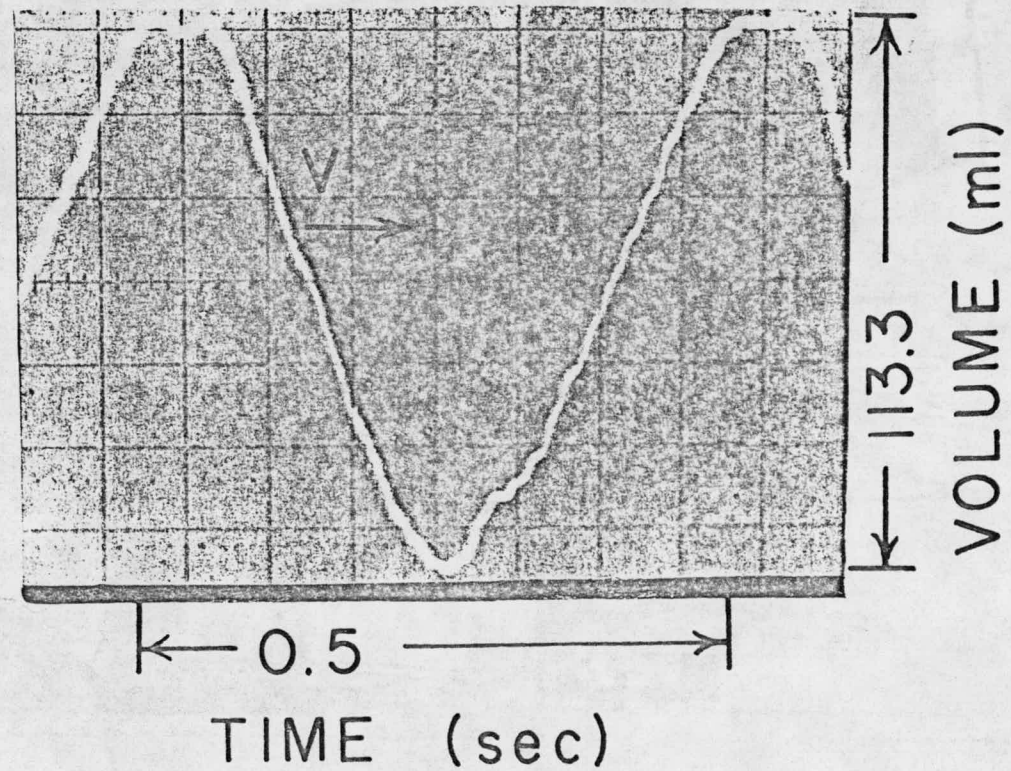
FIGURE X-10 : Function curves for AEC Bench Model Blood Pump

FIGURE X-11



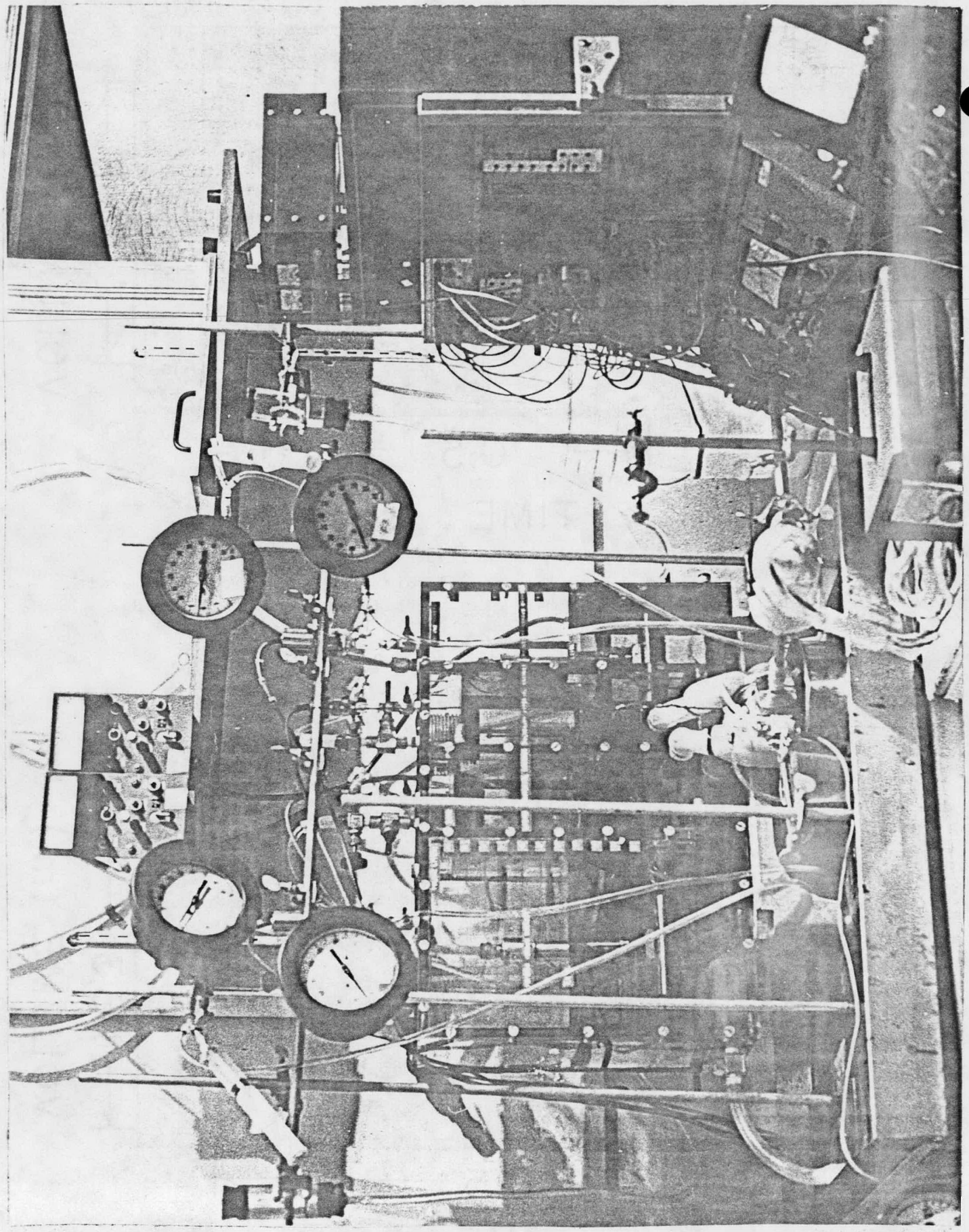
Left ventricular pressure and volume as a function of time with an output of 6.7 L/min mean arterial pressure of 100 mm Hg.

Figure X-12



Left ventricular volume as a function of time with an output of 10.3 L/min and mean arterial pressure of 100 mm Hg.

FIGURE X-13



Mock circulatory system with the heart attached as in Figure

IN VITRO STUDIES AND EXPERIMENTS

2. Thermal Dissipation from the Implantable Electric Motor

To determine the amount of heat dissipated from the implantable electric motor, two experiments were conducted to measure the heat loss from the motor under normal operating conditions.

An Electrocraft Series 550 electric motor and controller was connected to the Blood Pump and operated on a Donovan mock circulation system with a 12 inch flexible drive shaft between the electric motor and pump.

Indirect Approach: The Donovan mock circulation system was adjusted such that the blood pump maintained 100 mm Hg outflow pressure and 10 mm Hg inflow pressure. When cardiac outflow was approximately 11 liters/minute, current and voltage measurements were taken of the power into the electric motor after it had been run sufficiently long to stabilize (about 15 minutes). Voltage and current measurements gave the power input to the electric motor. Torque (in. - lbs.) and R.P.M. measurements provided the power output of the electric motor. The difference between the power input and power output was attributed to the heat losses from the electric motor. Small mechanical and electrical field losses were ignored.

For the electrical measurements:

Power input = Pi = IV = 18.90 watts: where

I = current

V = voltage

Power output = P_o = (torque (in.-lbs.) x r.p.m. x 10.65) = 8.52 watts

Difference (P_i - P_o) approximately equal to heat loss:

18.90 watts - 8.52 watts = 10.38 watts

(power input - power output = heat loss)

To confirm these measurements the test conditions were repeated with the implantable electric motor placed in a Dewar flask with 3,500 gm (7.709) of water. The Dewar flask provided thermal insulation for the water bath. The water bath and electric motor were initially equilibrated with the room temperature overnight. The motor was then operated 15 minutes to equilibrate with the water bath. Measurements were then made of the temperature rise in the water bath as a function of time while the electric motor was operating under the test condition specified earlier. By calculating the temperature rise for a given time period with a specified mass of water, the thermal energy dissipated from the electric motor imparted to the water bath environment was calculated.

Since 1 watt = 0.05688 BTU/minute and 1 BTU = amount of energy to raise 1 lb. of water 1° F, then from Figure X-14 it is seen that after the motor has equilibrated thermally (warmed up) the curve of temperature rise (Δ T) versus change in time (Δ t) is fairly linear. From this experimental data the heat loss was determined to be 9.04 watts. This value compares reasonably well with the analytical measurement of 10.38 watts. The experimental value of 9.04 watts is more likely correct however. The least accurate measurements are those of torque and r.p.m. which were made electrically and probably are only accurate to within 10 percent of the correct value.

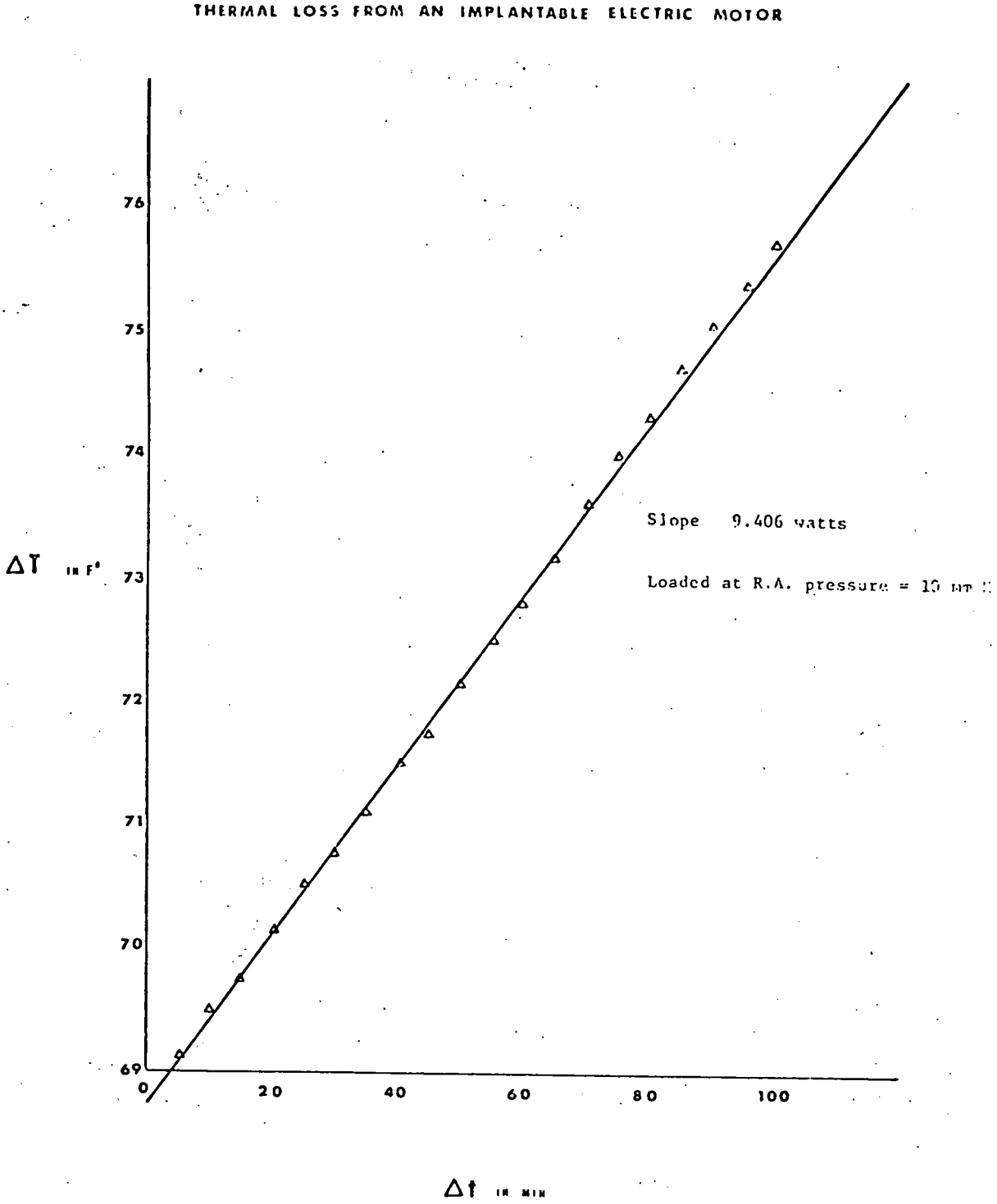


FIG. X-14: Thermal loss from implanted electric motor.

In Vitro Studies and Experiments

3. Coolant System for Implantable Electric Motor

Evidenced in the implantation experiments was the need to cool the small implantable electric motor used to drive the blood pump. Heat flux measurements indicated that as much as 9-10 watts of excess heat was dissipated by the electric motor when driving the blood pump implanted in a calf. The first attempt using the electric motor completely implanted in the calf's abdomen showed some local tissue damage resulting from hot spots on the electric motor casing.

One possible means of reducing the heat flux was to increase the surface area that dissipates heat. However, with 10 watts of heat to dissipate this alternative was not realistic. The solution employed was to wrap a copper cooling coil completely around the electric motor and flow water through the coil to maintain the electric motor at or near the calf's body temperature. The cooling coil was insulated from the body tissue with a Silastic rubber coating (see Figure X-15) which was overlaid with a Dacron velour layer to allow for tissue ingrowth. The water coolant line capacity was approximately 600 ml/minute and this line was bundled together with electric motor power lines, vacuum line and transducer leads. The bundle was sealed with silicone RTV, a medical grade rubber, and covered with Dacron velour. The bundle exited the calf's side near the abdomen, eliminating leads through the chest wall.

Initial experiments utilizing the cooling coil with a similar external heat exchanging coil controlled the heat dissipation to the calf at less than 0.5 watt. This heat flow coupled with a surface area of the electric motor and coil of approximately 400 cm^2, yield a heat flux of less than 0.001 watt/cm^2. Heat dissipation could be reduced to zero or even to the point where the motor temperature was cooler than the calf's body temperature if desirable.

However, it appeared satisfactory to maintain the electric motor to within $\pm 1^{o}$ C of the calf's body temperature. This was easily done by allowing the external cooling coil heat exchanger to radiate its heat to the ambient air. Cooling water flow rates of 400-600 ml/min. were found to be sufficient.

This cooling technique allowed for adequate cooling of the electric motor and also allowed the surface area of the motor package to be kept at a minimum. A Thermistor was permanently attached to the electric motor to continuously monitor the electric motor temperature as part of the experimental evaluation of the blood pump.

Figure X-16 provides a photographic view of the tissue cavity produced by the presence of the electrical motor in the abdomen of the calf. A pathological examination at autopsy revealed hyperemia and increased vascularity resulting from surgical trauma of the implantation of the electrical motor contiguous to the peritoneal wall.

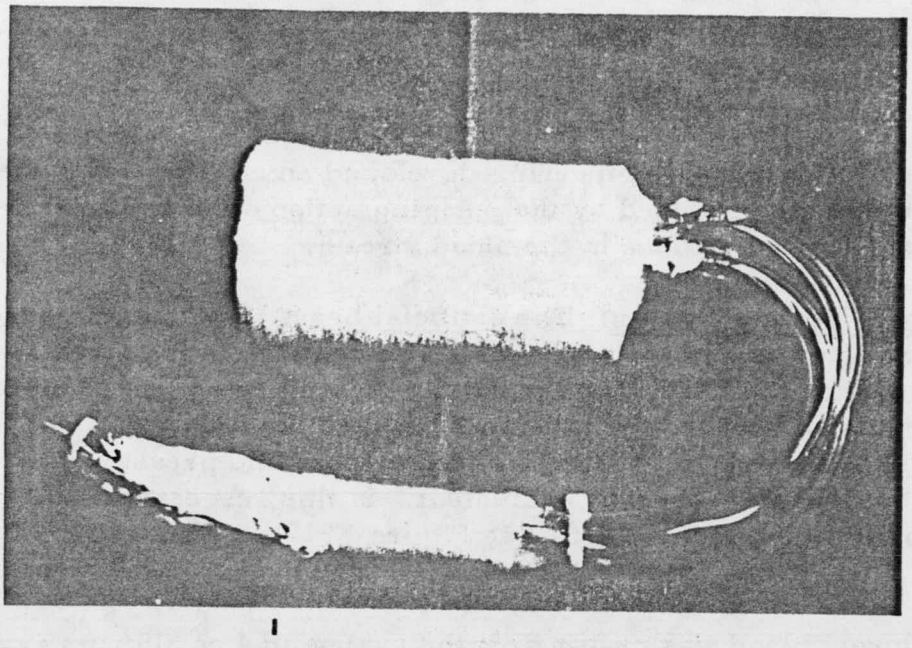


Figure X15: Variable electric motor prior to implantation. Motor has a tightly wound copper cooling coil covered with Silastic rubber insulation and wrapped with an outer layer of Dacron velour. Power and vacuum lines also are bundles and wrapped with Dacron velour.

Figure X16: Photograph taken from left side looking through evicerated abdomen to right peritoneal wall lining. Outlined shape is electric motor which at autopsy evidenced hyperemia and increased vascularity, resulting from surgical trauma and pressure of electric motor against the peritoneal wall.

In Vitro Studies and Experiments

4. Blood Pump Hemolysis Studies

The Institute of Biomedical Engineering developed an in vitro test to measure the amount of blood damage produced by the pumping action of an artificial heart ventricle and the presence of a foreign surface in the blood stream.

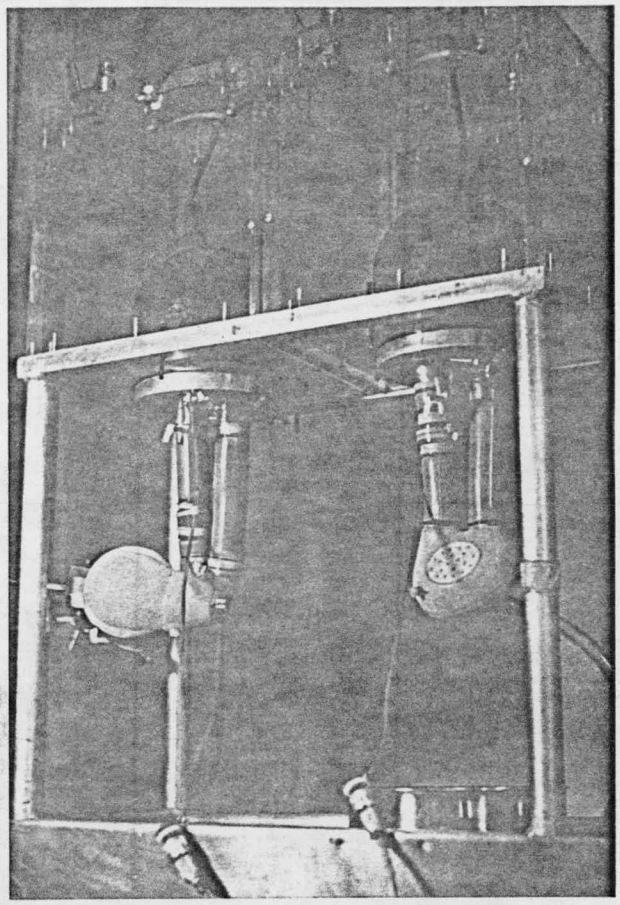
The Hemolysis Testing System: The artificial heart ventricle was attached to a Silastic bag which acted as a blood reservoir. The ventricle was driven as it would normally be in vivo. For the ERDA blood pump the driving rate was 120 beats per minute. A flow probe was situated between the reservoir bag and the inflow valve of the ventricle. The filling pressure of the system at standard temperature and pressure conditions was 40 mm Hg and the outflow pressure was equivalent. In this respect test conditions closely resembled those found in the right heart. See Figure X-17 for illustration of the hemolysis testing system.

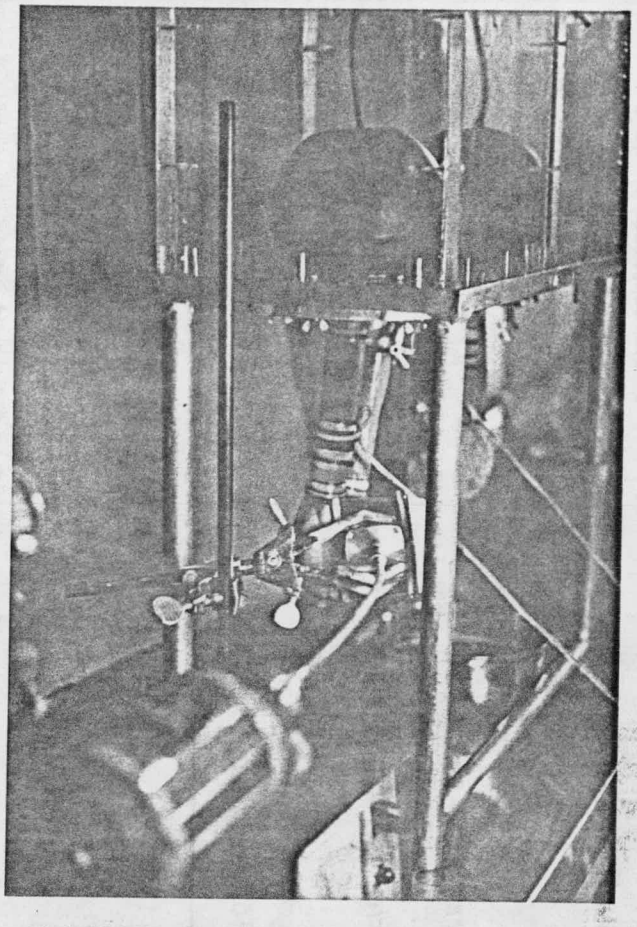
Test Procedure: Blood was drawn from the system in 4 cc aliquots every ten minutes. Each sample was centrifuged for thirty minutes and the plasma removed for analysis. The sample was analyzed for oxyhemoglobin, the substance which is released during hemolysis. A Cary model 41 spectrophotometer was used to scan the sample between 600 nanometers and 560 nanometers. The graph paper was calibrated with human blood so that the area measured under the scan peak was multiplied by 1.68 to yield data in mg% free plasma hemoglobin. The mg% value for each aliquot was then analyzed on the computer to find the slope and the slope correction. Another computer program was used to determine the hemolysis index.

The hemolysis index HI was defined as follows:

$$HI = \frac{(Slope)\ (100-Crit)\ (Vol-1)}{Flow \times 10^2}$$

Results: The hemolysis index data obtained for the ERDA blood pump ventricle were very low. The pump produced less blood damage as measured by the Hemolysis Index (0.008) than any other ventricle tested at the Institute. In comparison, the Kwan-Gett 8 cm smooth ventricle had a mean value for HI of 0.02 at a driving pressure of 6 psi, 35% systole and 100 beats per minute. The Jarvik Ventricle had a value of 0.072 at the same driving parameters. These values represented the same range of flow values as those used in testing the AEC blood pump. See Table X-5 for specific data.





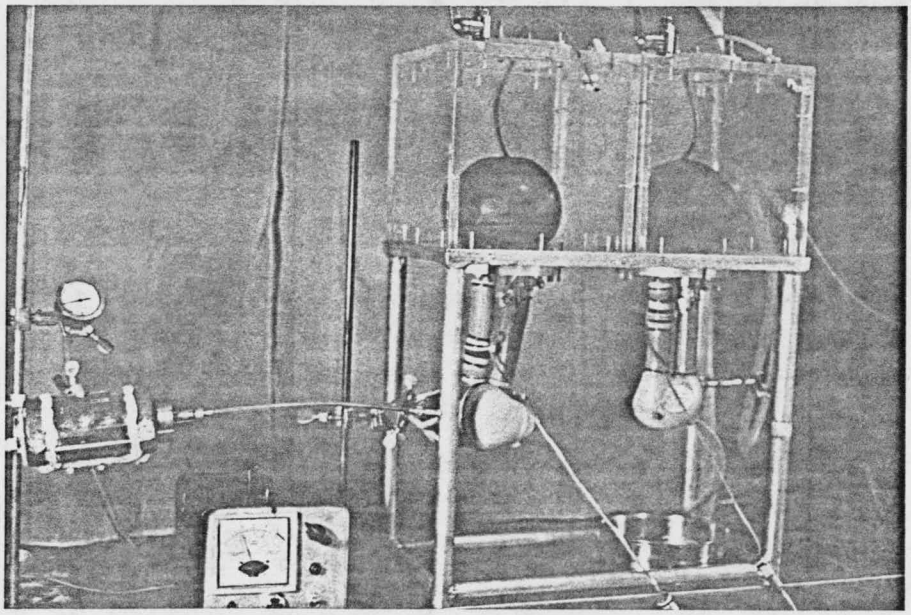


Figure X-17: In vitro hemolysis testing equipment used for testing ventricles for blood damage.

TABLE X-5

HEMOLYSIS TEST RESULTS FOR AEC BLOOD PUMP VENTRICLES

	Change Mg. % Hb	HI	Slope	Slope-Corr.	Hct.	Flow	BPM	Run Time (Hrs.)
AEC Smooth Heart (Silastic)	9.6	.00553	.0655	.841	49	13.3	120	2
	5.1	.00404	.0428	.935	43	13.3	120	2
	6.8	.01113	.1160	.981	42[a]	13.3	120	1
	5.9	.00996	.0941	.979	36	13.3	120	1
	6.1	.00913	.0936	.972	41	13.3	120	1
	4.8	.00803	.0837	.962	42	13.3	120	1
	10.2	.00744	.0934	.980	50	13.8	138	2
Mean	6.38	.00790	.0826	.945	42.2			
S.E.	.707	.0011	.0104	.0219	1.70			
Standard Deviation	1.73	.0027	.0255	.0536	4.17			

[a] Donor blood sample

In Vitro Studies and Experiments

5. Evaluation and Modification of IVBM Ventricles against Standard Performance Criteria

To provide a standard performance criteria for evaluating the IVBM ventricle performance, an ideal performance standard or desiderata for the blood pump performance was established for the calf as shown in Figure X-18, "Desiderata of Mock Circulatory Hemodynamics for ERDA Blood Pump." In this figure cardiac output, pulmonary artery pressure, aortic pressure and left atrial pressure are defined for idealized performance as a function of right atrial pressure. Also, an acceptable band of deviation for each of these variables from ideal is given by the dashed curves enclosing the ideal curve. Using this figure as a basis for evaluating performance, a systemic approach was pursued to determine acceptable system variable behavior and design modifications required to provide optimum performance of the IVBM blood pump on a mock circulation system.

Figures X-19 and X-20 indicate the typical performance of an unmodified IVBM blood pump with Silastic ventricles and four Bjork-Shiley valves in inflow and outflow positions. Comparing actual performance data in these figures with ideal performance given in Figure X-18, it was observed that pulmonary artery and pulmonary venous pressures increased sharply with increase of right atrial pressure. Also, cardiac output at low right atrial pressures was higher than necessary. After careful analysis a primary cause of this imbalance in performance was attributed to the observation that under general conditions the right ventricle outpumped the left ventricle, resulting in the elevated pulmonary pressures. The compliance (i.e. rate of change of volume with pressure, $\frac{\partial V}{\partial P}$) was determined for each ventricle and it was found that during systole at high arterial pressures, the left ventricle would distend more than the right ventricle and thus the net output from the left ventricle was reduced, allowing the right ventricle to outpump the left ventricle. This imbalance in pumping output resulted in increased pulmonary artery and venous pressures, as the right atrial pressure increased.

Various design modifications of the standard Silastic ERDA blood pump ventricles were made to realize a better balance between left and right ventricle output at high right venous pressures. One modification performed was coating the outside surface of the left outflow tract with fiberglass to make the tract less distensible during systole.

The performance of a Silastic ventricle with a fiberglass outside coating is shown in Figure X-21. Reducing the compliance of the left ventricle does result in lower pulmonary arterial and venous pressures.

Another design modification made was to reduce the displacement volume of the right ventricle which should result in less pumping output from the right ventricle. This modification referred to as the delta V (i.e. volume V reduced by an amount ΔV) ventricle was tested in vitro and the results are given in Figure X-22. The delta V ventricle was slightly better in lowering pulmonary arterial and venous pressures than the modification of coating the left outflow tract with fiberglass.

It is also important to observe that although pulmonary arterial and venous pressure were reduced by these modifications the cardiac output of the ventricles was still flat (i.e. at low right atrial pressures in the range of -10 to 5 mm Hg, the output was higher than desirable). This meant that the ventricles were not sufficiently compliant under diastole and the ventricles tended to suck from the venous return during diastole. Therefore, an additional modification to the Silastic ventricle was made by making the ventricles very compliant for diastole and maintaining the rigid outflow tract over the left ventricle to reduce compliance during systole. The comparative performance of the ventricles with these modifications is shown in Figure X-23. The increase in diastolic compliance was accomplished by fabricating improved Silastic ventricles with ventricle domes 0.030 inch thick. The standard (unmodified) Silastic ventricle for the ERDA IVBM oil-filled blood pump exhibited ideal range behavior for the (1) pulmonary venous pressure when the right atrial pressure varied from -10 to -5 mm Hg, (2) pulmonary arterial pressure when the right atrial pressure varied from -10 to 0 mm Hg and (3) cardiac output for right atrial pressures varying from 10 to 20 mm Hg. It is seen from Figure X-23 that the best combination of modifications exhibited ideal range behavior for right atrial pressures, varying from about -3 mm Hg to 30 mm Hg. This system employed Silastic ventricles with thin domes, a rigid left outflow tract and a reduced volume (Δ V) right ventricle.

A summary of the effects upon ventricular performance of all these modifications as a function of right atrial pressure is shown in Figures X-24 to X-28. Figure X-24 displays the performance of the modified ERDA ventricle as a function of flexible shaft speed in RPM. Figure X-25 indicates the behavior of cardiac output as a function of aortic pressure. Figures X-26 through X-20 display the complete modified ERDA ventricle performance for 3 different aortic outflow pressures.

An investigation into the effect of orientation of the Bjork-Shiley valves upon ventricle performance was also performed by in vitro testing. Various tests were conducted using the standard Silastic ERDA ventricles and results are given in Figure X-29. The general conclusion made was that within the statistical uncertainties of the sampling, Bjork-Shiley valve orientation had little effect upon pulmonary arterial and venous pressures.

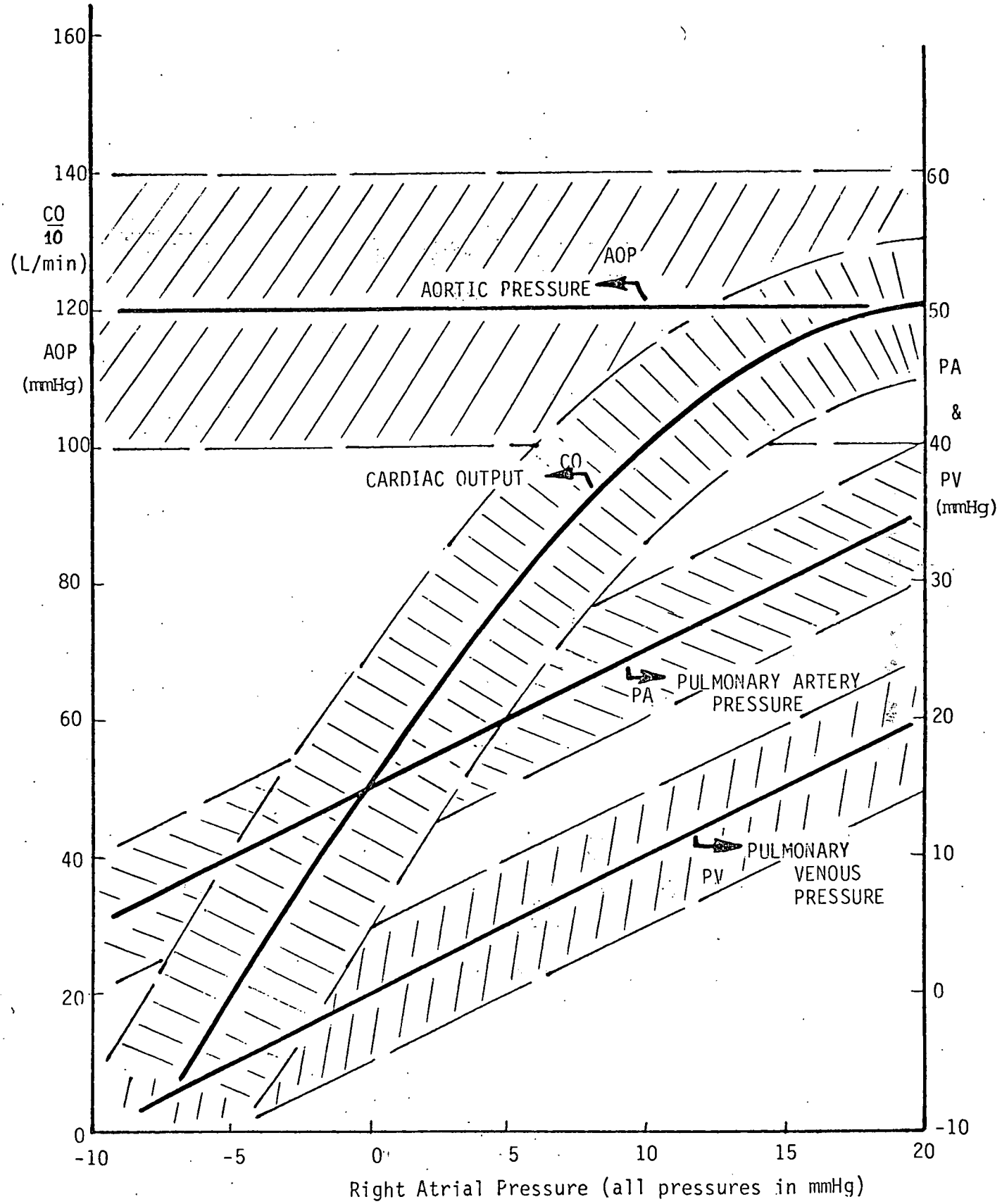


Figure X-18: Desiderata of Mock Circulatory Hemodynamics for ERDA Blood Pump. Present pump meets these requirements.

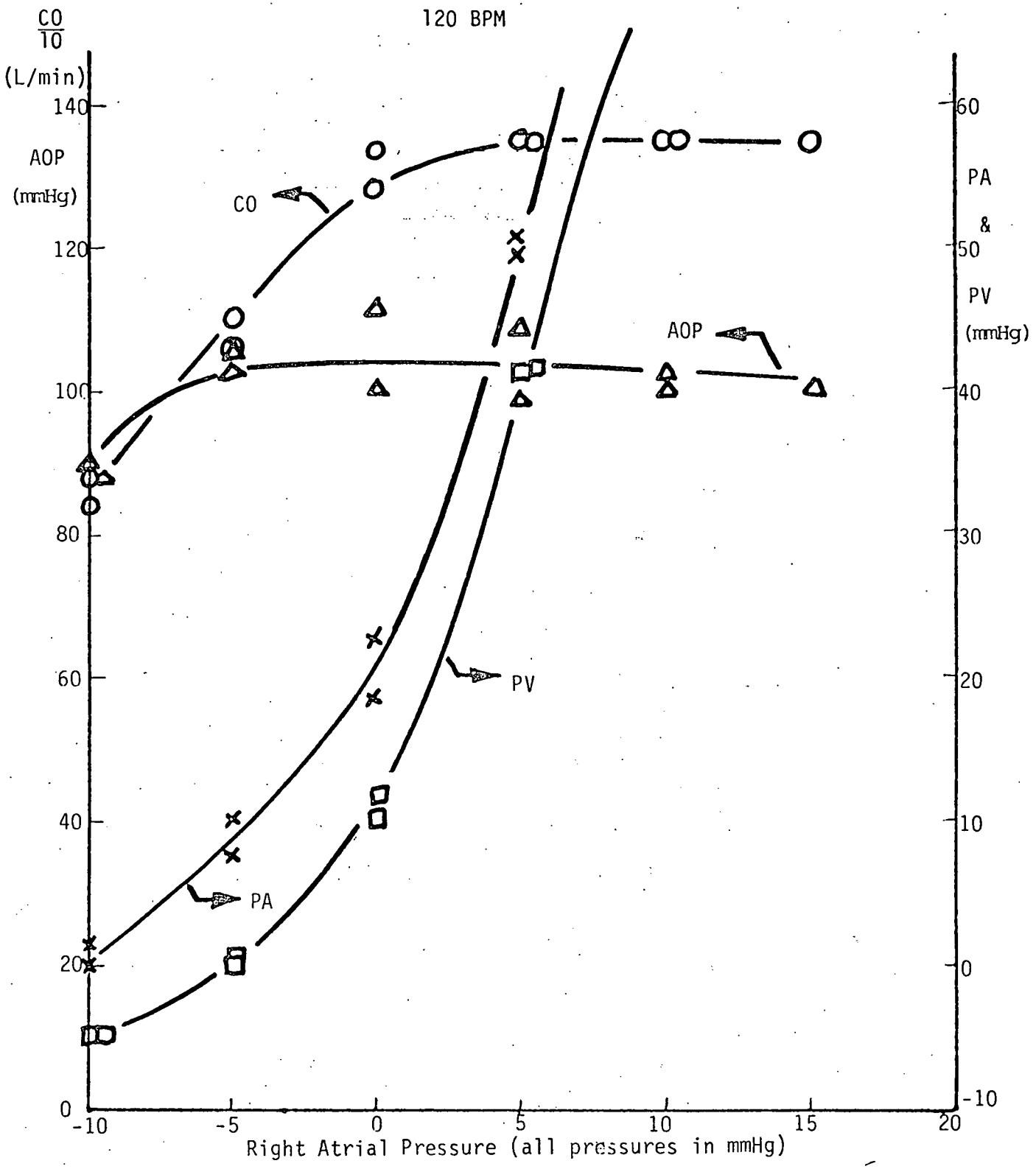


Figure X-19 Performance of ERDA Blood Pump with Standard Silastic Ventricles and 4 Bjork-Shiley Valves, all in the No. 2 Position.

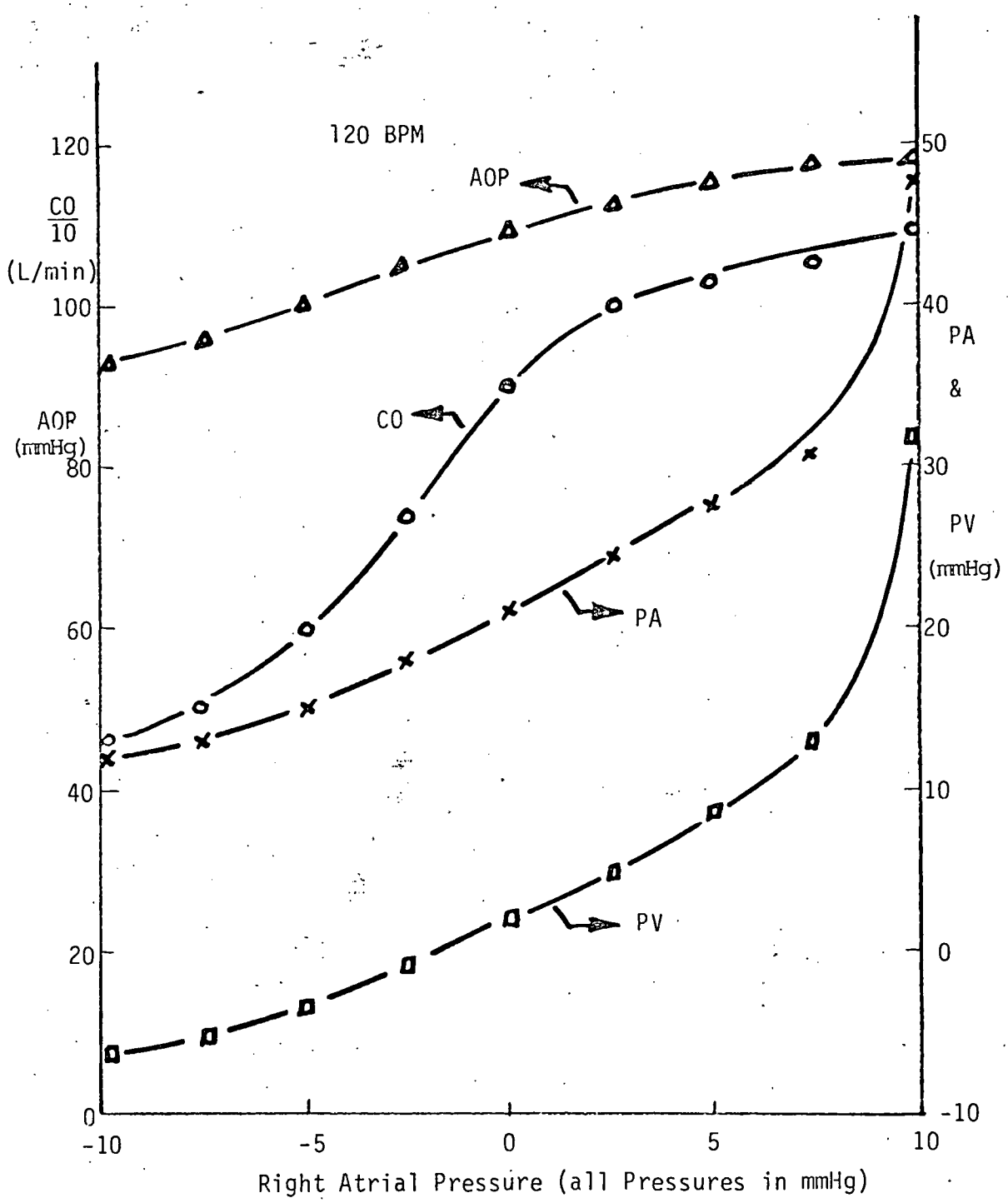


Figure 20: Performance of ERDA Blood Pump with Standard Silastic Ventricles and 4 Bjork-Shiley Valves (Outflow in No. 2 Position and Inflow in No. 4 Position).

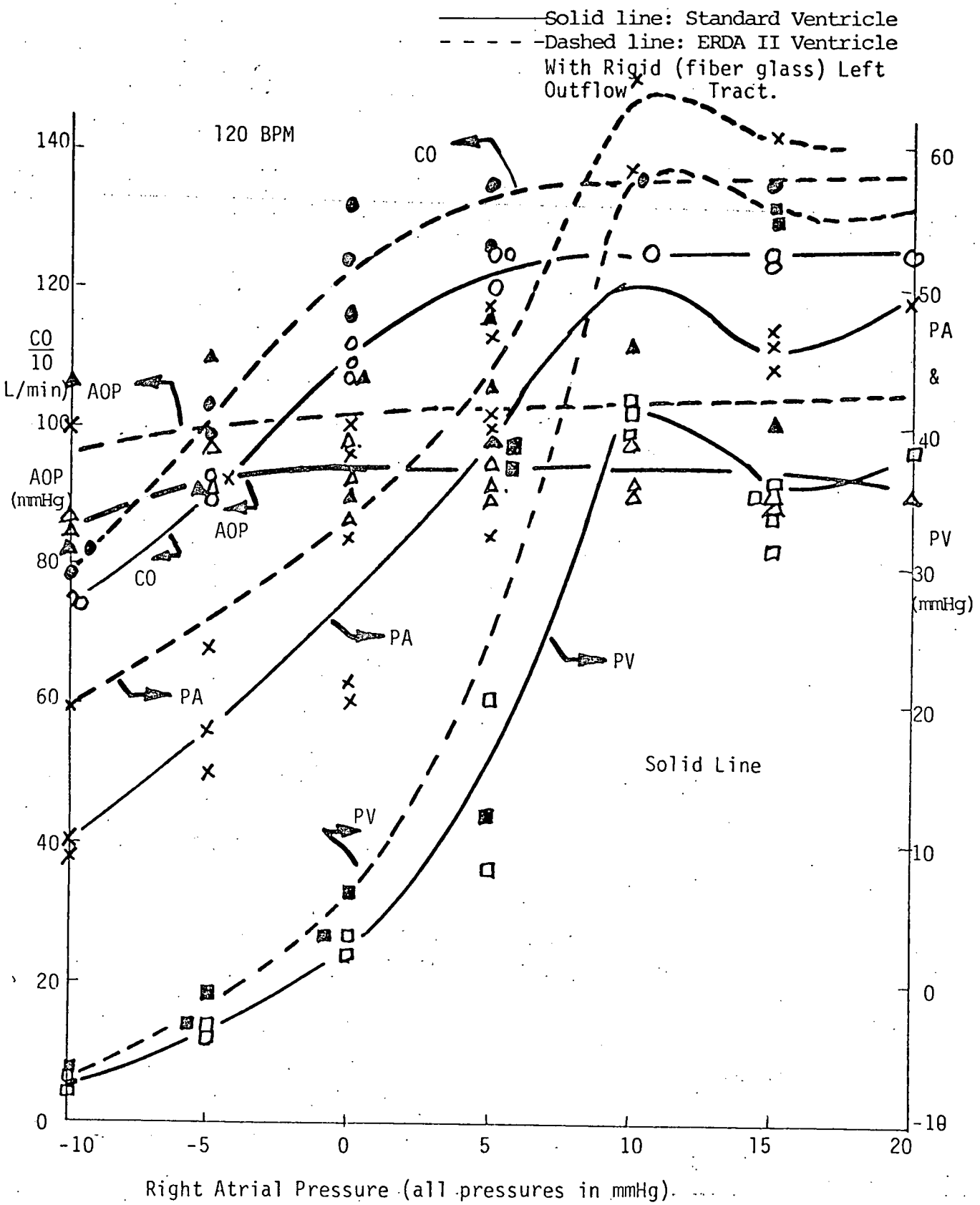


Figure X-21: Performance of ERDA Blood Pump with Rigid Left Outflow Tract.

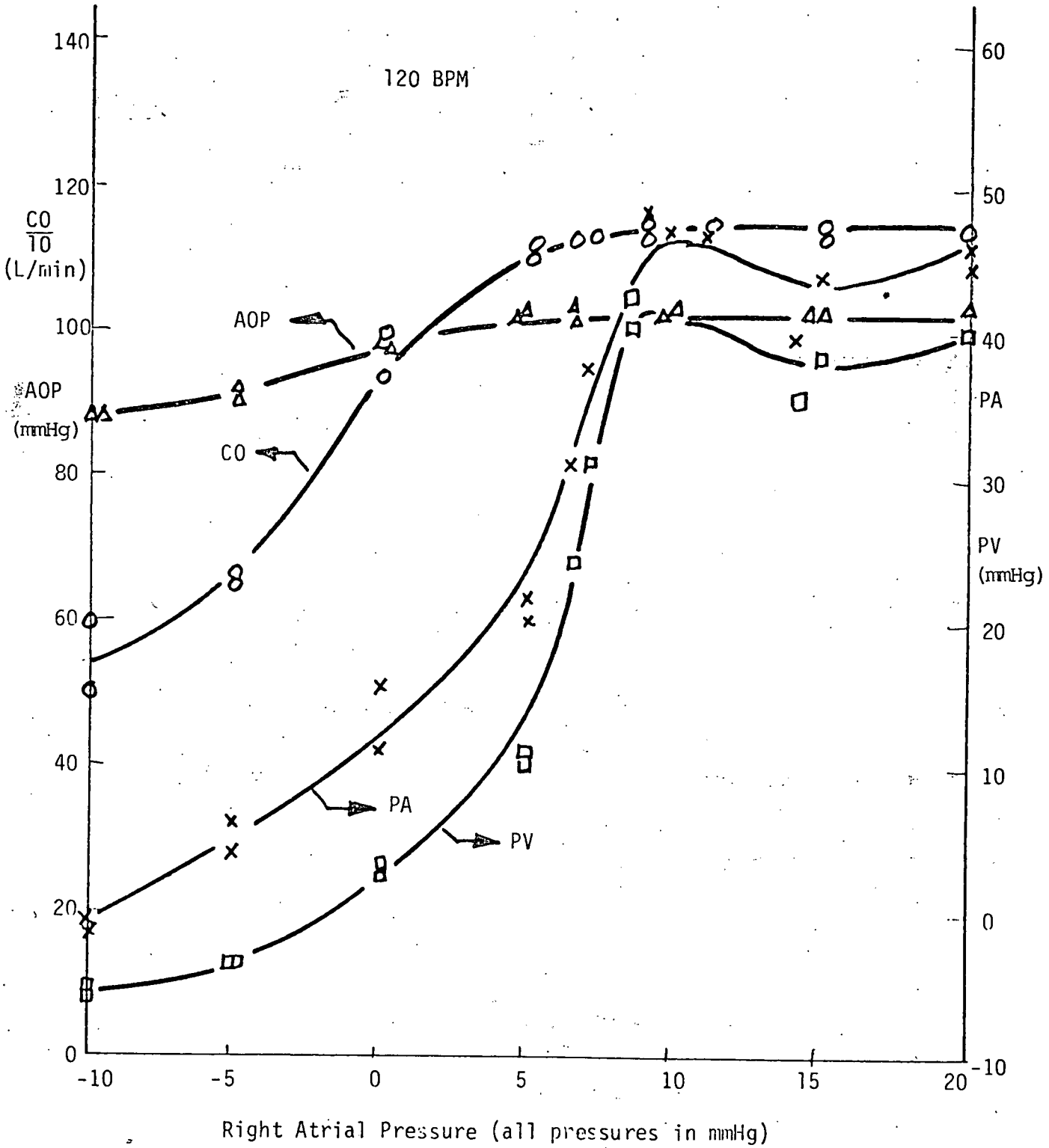


Figure X-22 Performance of ERDA Blood Pump with ΔV Right Ventricle and Rigid Left Outflow Tract.

120 BPM

_____Solid Line: Standard Ventricles

- - - -Dashed Line: ERDA II Ventricles

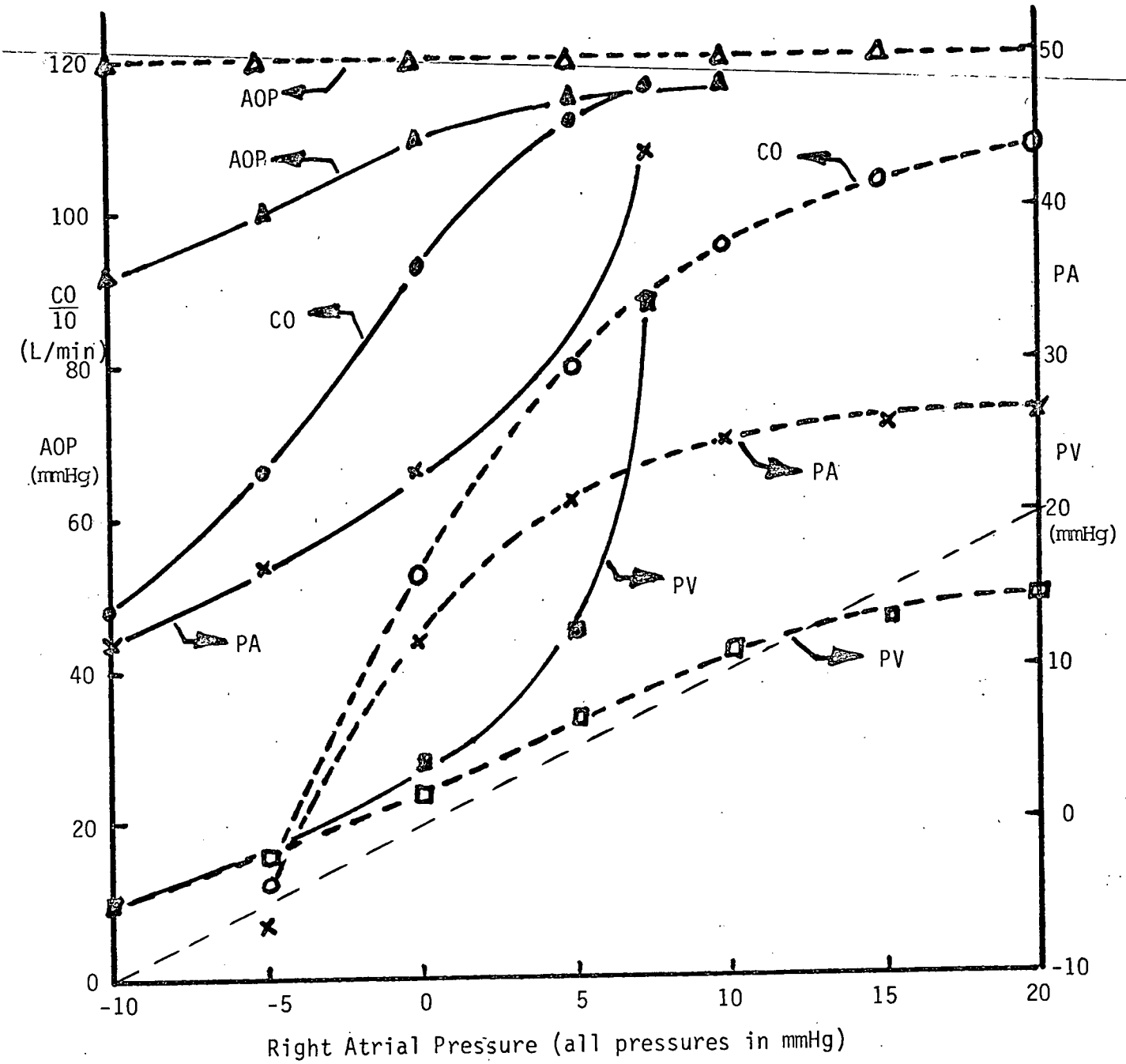


Figure X-23 Performance of ERDA Blood Pump with Standard Ventricles (4 Bjork-Shiley Silastic Valves in No. 2 Position) compared to modified ERDA II Ventricles (30 mil thick Silastic Domes, 4 Bjork-Shiley in No. 2 Position Except Left Outflow in No. 4 Position, ΔV Right Ventricle).

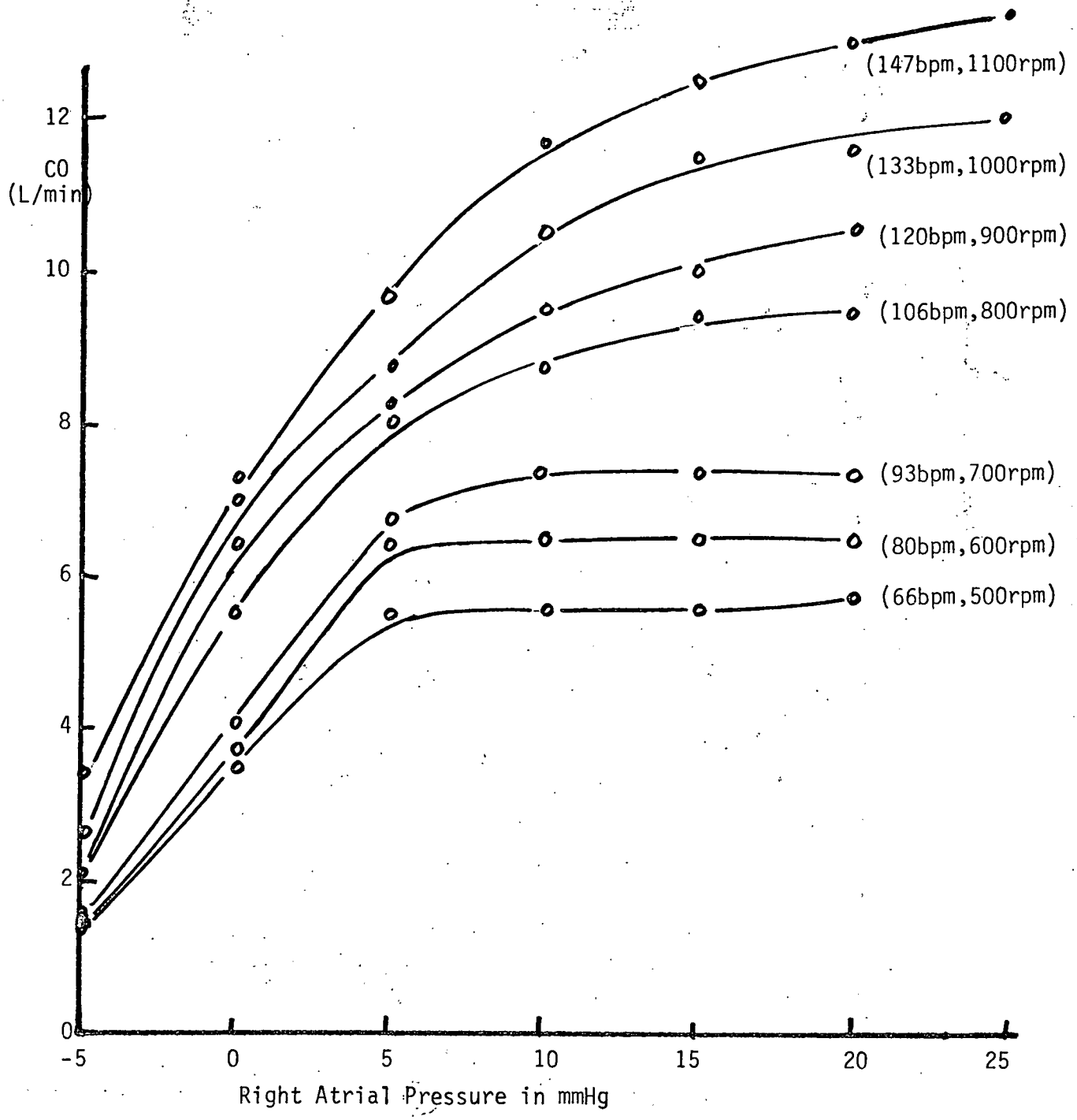


Figure X-24 Output of ERDA Blood Pump (Silastic ERDA II Ventricles with ΔV Right Ventricle and 4 Bjork-Shiley Valves) as a Function of Flexible Shaft Speed in RPM.

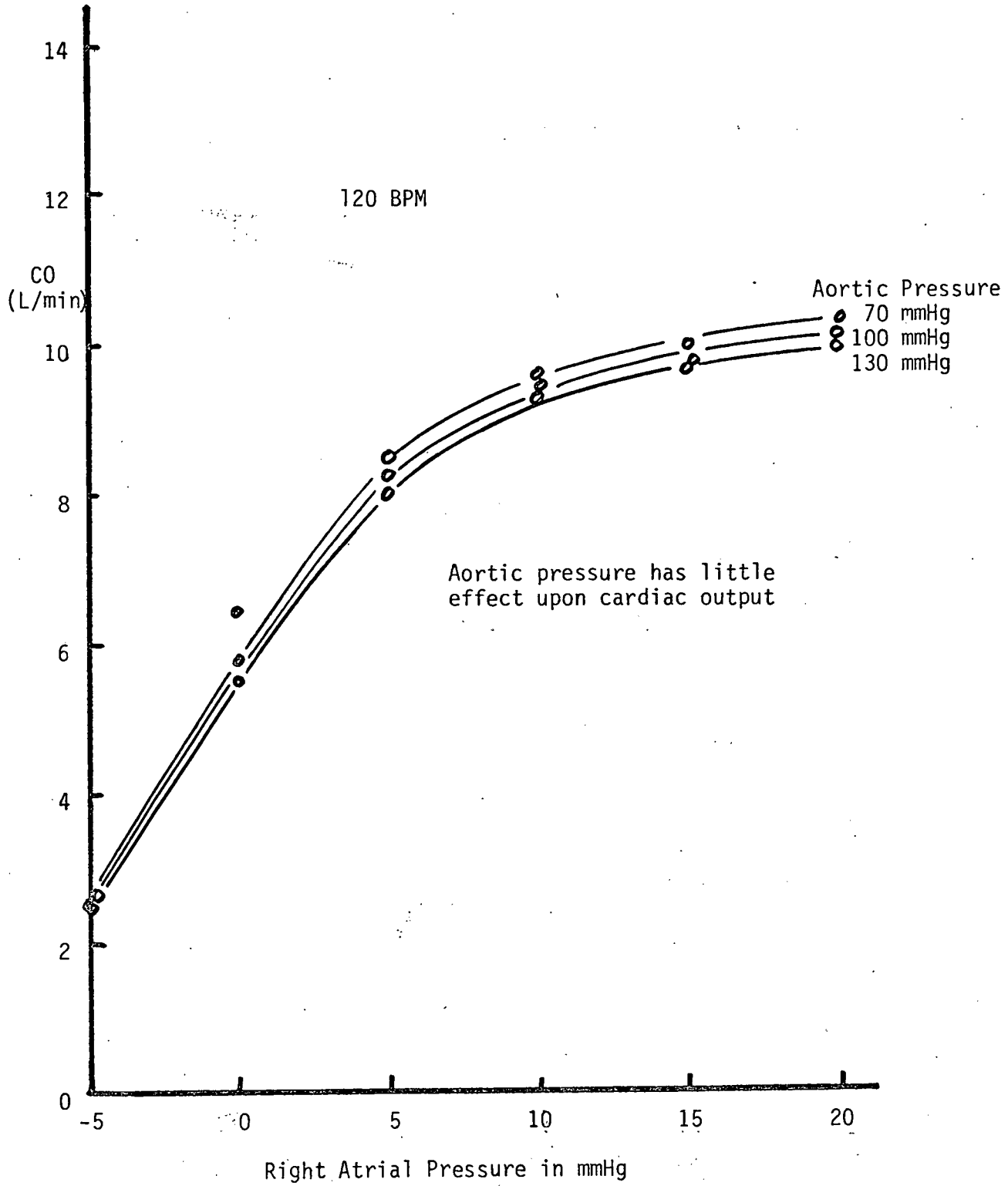


Figure X-25 Output of ERDA Blood Pump (Silastic ERDA II Ventricles with ΔV Right Ventricle and 4 Bjork-Shiley Valves) as a Function of Aortic Pressure.

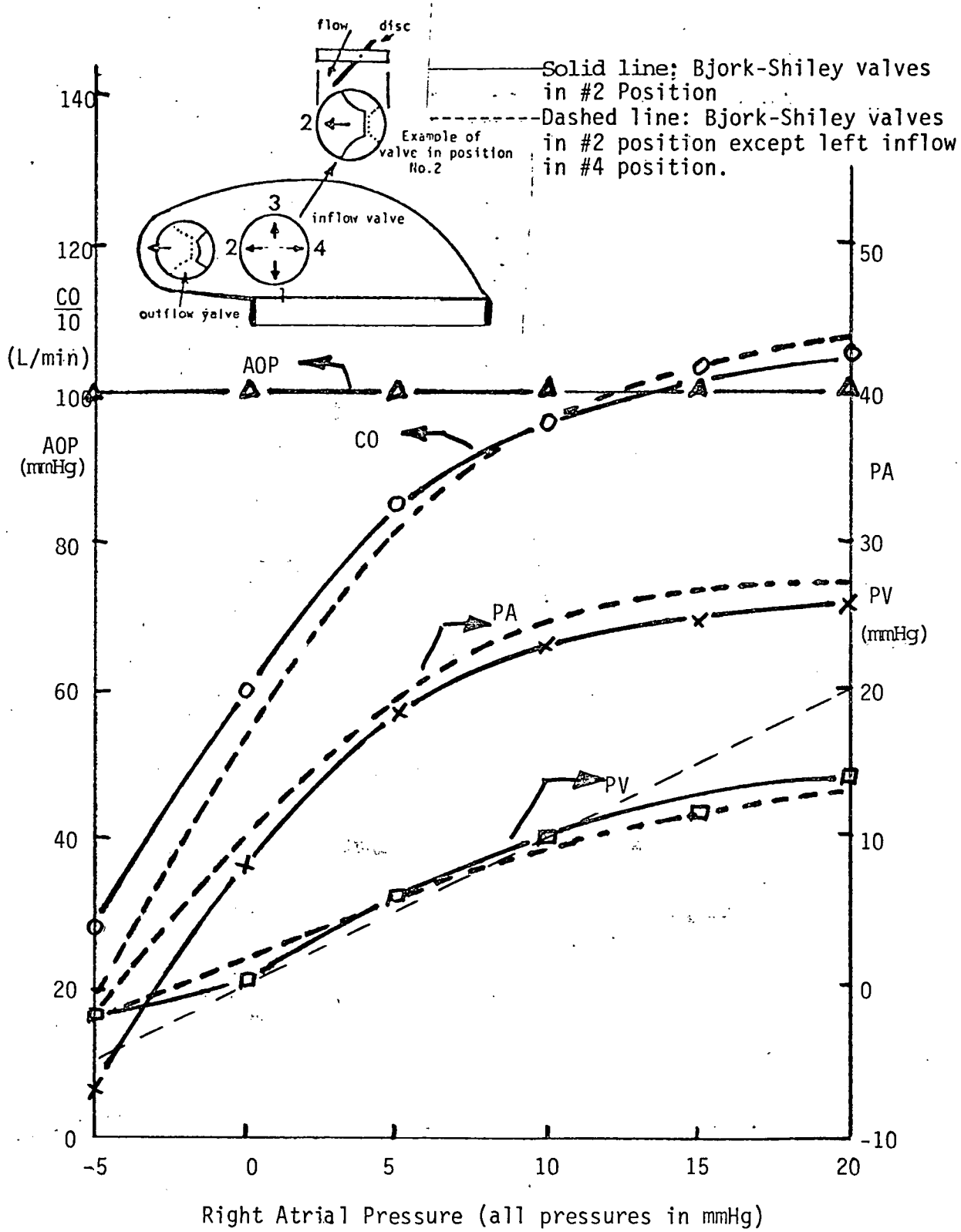


Figure X-26: Performance of ERDA Blood Pump (Silastic ERDA II Ventricles with ΔV Right Ventricle and 4 Bjork-Shiley Valves) for an Aortic Outflow Pressure of 100 mm Hg.

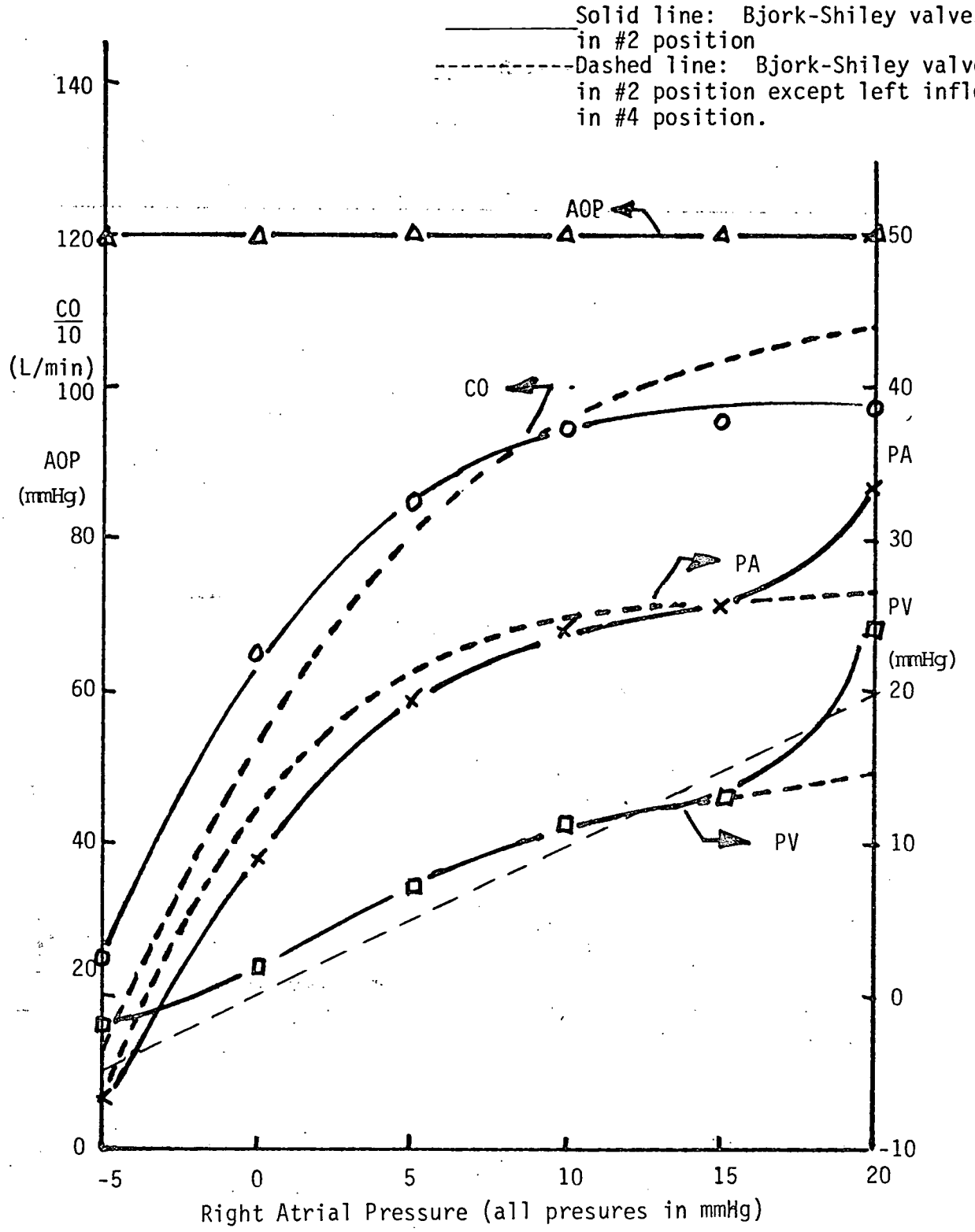


Figure X-27: Performance of ERDA Blood Pump (Silastic ERDA II Ventricles with ΔV Right Ventricle and 4 Bjork-Shiley Valves) for an Aortic Outflow Pressure of 120 mm Hg.

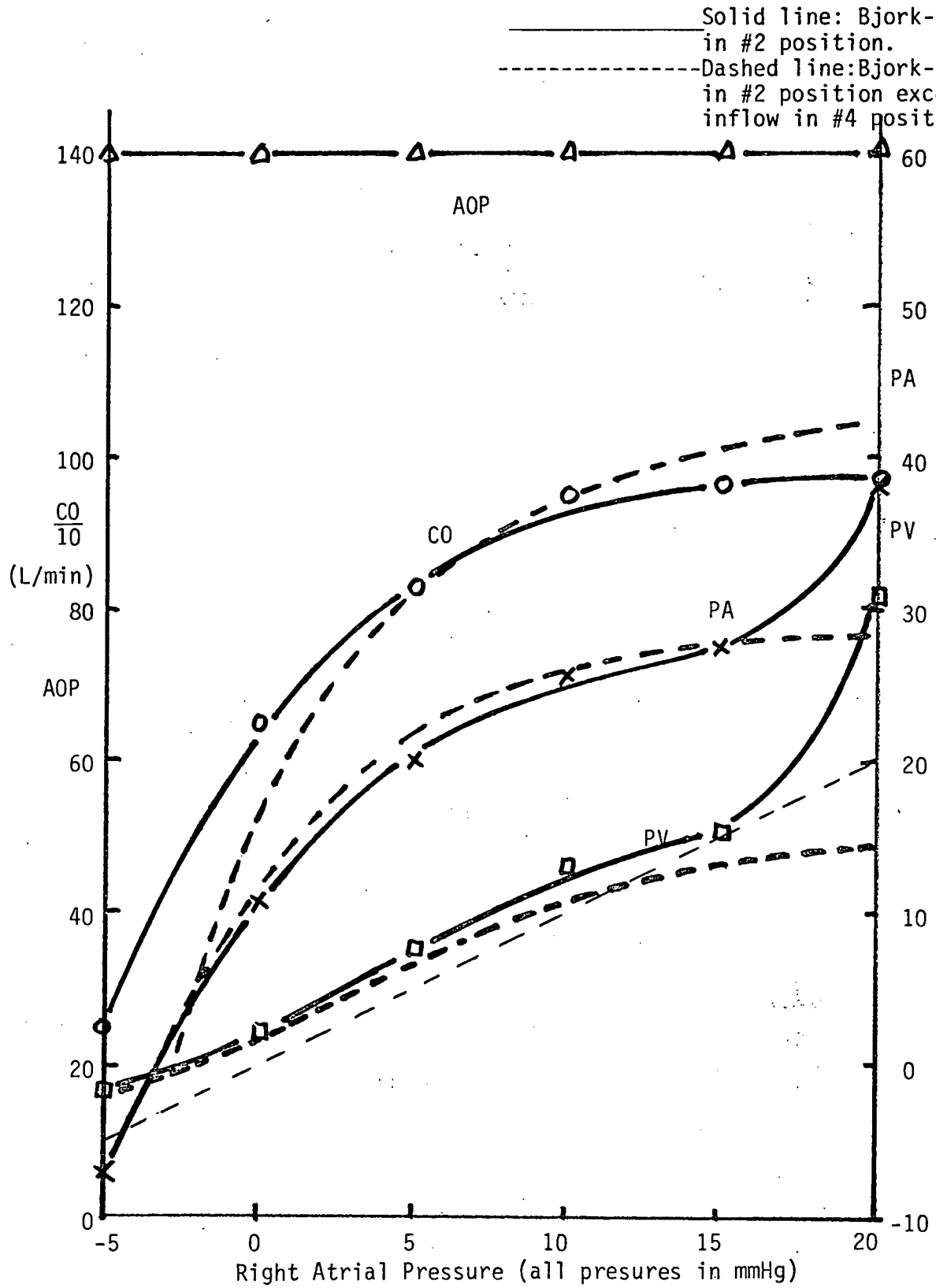
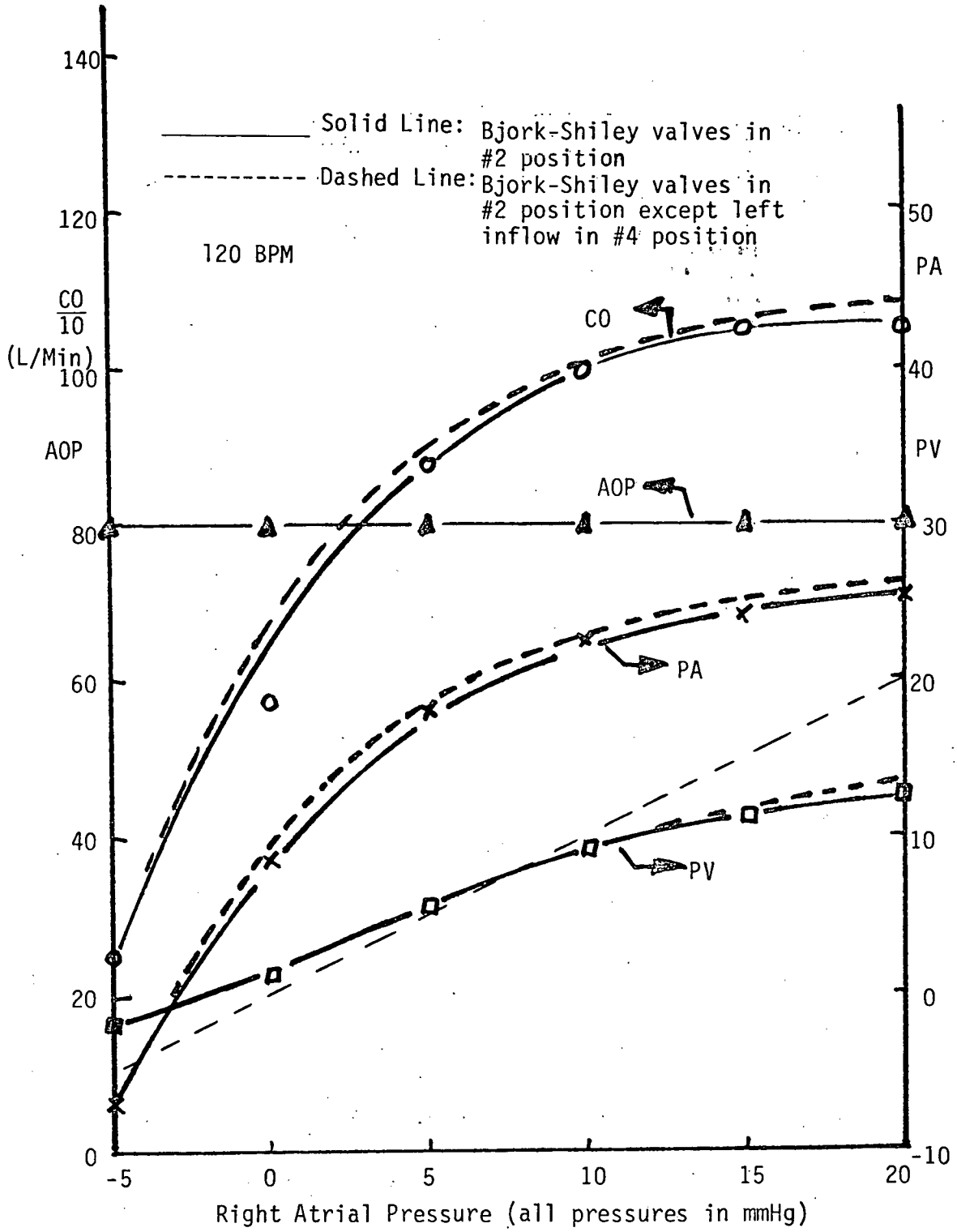


Figure X-28: Performance of ERDA Blood Pump (Silastic ERDA II Ventricles with ΔV Right Ventricle and 4 Bjork-Shiley Valves) for an Aortic Outflow Pressure of 140 mm Hg.



FigureX-29: Performance of ERDA Blood Pump (Silastic ERDA II Ventricle and 4 Bjork-Shiley Valves) as a Function of Inflow Valve Rotation.

XI. IN VIVO STUDIES AND EXPERIMENTS

1. Synopses of Selected In Vivo Experiments with the DOE Artificial Heart System

During the tenure of the DOE Contract, the Institute for Biomedical Engineering performed 56 in vivo experiments in which various sub-systems of the DOE Artificial Heart system were implanted in calves. Synopses of important, "bench-mark" experiments are provided to indicate the evolutionary progress made during the contract in pre-surgical, surgical and post-surgical methods, techniques and protocols as they were iteratively developed, evaluated and improved.

Summary of Total Heart Replacement Experiment No. 1 (TH73C16D15AEC1, June 12, 1973):

The purpose of this initial experiment was to resolve surgical problems, determine hemodynamic response of the heart, determine power requirements of the heart, and determine mechanical blood damage created by the heart. The animal used was a Holstein calf weighing approximately 100 kg and the experiment was performed on June 12, 1973. Surgical preparation of this animal went well; however, at the time of attempting to place the heart into the animal it was not possible to close the quick connects. Therefore, the animal died on the table without being pumped. No autopsy was performed on this animal.

Summary of Total Heart Replacement Experiment No. 2 (TH73C15D14AEC2, June 14, 1973):

The purpose of this experiment was to resolve surgical problems and to determine the hemodynamic response of the heart, mechanical blood damage, and power requirements. The animal used was a Holstein calf weighing approximately 100 kg, with an externally located driving system. This animal went into fibrillation upon opening of the pericardium. Attempts to defibrillate were unsuccessful and partial bypass was achieved approximately 20 minutes after fibrillation, leaving the animal without significant neurological function. The decision was made to implant the heart, nevertheless, for practice and fitting of the blood pump. An attempt was made to install the heart in this animal without benefit of quick connects and the total surgery time for implantation of the blood pump was two hours and 30 minutes. The chest was closed and the pump operated for a short time, and then turned off. No autopsy was performed on this animal.

Summary of Total Heart Replacement Experiment No. 3, (TH73C23B22AEC3, August 2, 1973):

The animal selected was a male Holstein calf weighing 95 kg. Surgical preparation on this animal went well. Bypass time was two hours and five minutes. The animal received the heart replacement quite well. Nine hours after total heart replacement the animal was able to stand. Unfortunately the animal expired when the flexible drive shaft broke 12 hours after heart replacement. It is believed that this drive shaft broke because it had been subjected to autoclaving and some damage had occurred to the shaft. At autopsy it was found that the heart fit well within the chest.

Summary Total Heart Replacement Experiment No. 4 (TH73C29B26AEC4, August 30, 1973):

Experiment No. 4 was a sterile, short-term study with the purpose of determining the blood compatibility of a smooth surface Silastic ventricle and establishing and evaluating initial surgical implant procedures.

Surgical Procedure:

A 107 kg male Holstein calf was used for the experiment and no preoperative antibiotics were administered. Bjork-Shiley 29 AxP inflow valves and 27 AxP outflow valves (viterous-carbon) were sealed into the ventricles and the entire blood pump

autoclaved prior to surgery. An external electrical motor drove the blood pump at 120 beats per minute. A sternum split surgical procedure was followed, using Brevane followed by Halothane as anesthesia. Surgery required 3½ hours during which the calf was sustained by a Bently heart-lung machine for 137 minutes. Because of the short-term nature of the experiment, blood chemistry, hemolysis, clotting times and driving pressure parameters were not monitored.

Postoperative Results:

Heparin was administered as an anticoagulant at a controlled rate. An initial pulmonary tidal volume of 1100 cc was recorded. The calf received mechanical ventilation support from a Bird respirator on 100% oxygen. Within a few hours after surgery, chest drainage totaled 600 cc. The calf remained motionless in a prone position for five hours at which time he held up his head. At five hours the calf was still receiving mechanical breathing support, but with only 65% oxygen. At seven hours an unsuccessful attempt was made to have the calf stand. At nine hours, 5 gm streptomycin was administered and mechanical breathing support was continued with 55% oxygen. At 10 hours the calf attempted unsuccessfully to stand. Penicillin was administered. From 11 to 13 hours the calf remained motionless, his chest drainage totaled 2300 cc and his todal volume increasing to 1650 cc. Respiratory support was maintained at 13 hours with oxygen concentration reduced to 45%. Auditory and visual reflexes were good, but at 13 hours after surgery the flexible drive shaft broke and the blood pump stopped.

Autopsy Results:

Autopsy of the calf indicated complete atelectasis in the left middle and right upper lobes and abnormal lung tissue full of granulomas. The lungs weighed 1.8% of total body weight, almost twice the normal value. Approximately 600 cc of clotted blood were found in the thorax. There were no mechanical problems associated with the ventricles or blood pump assembly. A broken drive shaft was the cause of death at 13 hours postoperative.

Summary of Total Heart Replacement Experiment No. 5 (TH73C35B32AEC5, September 27, 1973)

Experiment No. 5 was scheduled as a short-term, sterile experiment to determine the blood compatibility of a smooth Silastic ventricle and to further evaluate surgical implant procedures.

Surgical Procedures:

A sternum split procedure was performed on a 111 kg male Holstein calf, using Brevane followed by Halothane. Vitreous carbon Bjork-Shiley inflow (29 mm) and outflow (27 mm) valves were used on smooth Silastic ventricles. Ventricles and blood pump assembly were autoclaved prior to surgery. Surgery required four hours and the calf was sustained by a Bentley heart-lung machine for 134 minutes. Twenty-four hours prior to surgery the calf's lung functions were measured by a spirometer to determine normal preoperative tidal volume, oxygen uptake, minute volume and functional residual capacity.

Postoperative Results:

Because of the short-term nature of the experiment, hemolysis, clotting times and clotting factors were not monitored. Heparin was administered as an anticoagulant. Streptomycin was administered every five hours starting at 14 hours after surgery.

During the first ten hours the calf moved very little. Pulmonary tidal volume fluctuated about 200 cc but the mean value remained essentially unchanged. Chest drainage totaled more than 2200 cc, auditory and visual relfexes remained stable but poor. At 20 hours the calf unsuccessfully attempted to stand.

In the next ten hour period tidal volume fluctuated and gradually decreased to 1600 cc. Visual and auditory reflexes improved and remained good. Again the calf made several unsuccessful attempts to stand.

Mechanical ventilation was maintained and oxygen concentration was increased from 21% to 40%. Chest drainage increased. Approximately four liters total of fluid were recovered from chest drainage tubes.

From 20 to 30 hours reflexes remained good with little change in tidal volume. Chest drainage decreased to 1000 cc. Body temperature stabilized at 38^{O} C and mechanical breathing support continued at 20% oxygen. At 24 hours the calf stood unassisted for five minutes.

During the fourth ten hours increment chest drainage reduced to approximately 300 cc and tidal volume reduced to 1300 cc. At 40 hours both visual and auditory reflexes became poor. There was very little movement from the calf and mechanical ventilation was maintained, increasing oxygen concentration to 40% at ten liters per minute.

From 40 to 50 hours chest drainage decreased to 200 cc with a 200 cc increase in tidal volume. Auditory and visual reflexes improved and remained fair. Body temperature lowered to 37.7 ^{O}C and mechanical breathing support was continued. At 50 hours chest drainage tubes were removed.

At 51 hours the calf was extubated and breathing was spontaneous for approximately 20 minutes, but intubation again became necessary. A large increase in tidal volume to 1780 cc was monitored. Visual reflexes ceased and auditory reflexes remained fair. The calf's temperature increased to 39^{O} C and the calf remained quiet until the 60th hour.

At 65 hours eyelid reflex was absent and auditory reflexes were poor. Mechanical breathing support was increased to 50% oxygen and there was a 200 cc decrease in tidal volume. At 69 hours the calf was deliberately terminated.

Autopsy Results:

Autopsy performed upon the calf revealed enlarged lungs, weighing 1.7% of total body weight (compared to the normal 0.96%). Kidneys were found to be normal in weight but contained several large emboli. Small emboli were found in both lower lobes of the

calf's lungs, showing signs of congestion and atelectasis. The spleen was normal but the liver was enlarged and congested, measuring 2.76% of total body weight (compared to the normal 1.65%). Suture wires were unbroken but two thirds of the sternum incision was open, providing a tract for infection. 500 cc of clotted blood were found in the thoracic cavity with evidence of massive infection. The condition of the blood pump ventricles was tolerable with small clots located around the valve rings. Fibrin deposition was noted around suture lines of both the right and left atria. Firm clots were encountered around the housing and diaphragm junction. No mechanical problems were found but the Silastic covering around the drive line was cut. The flexible drive shaft showed no signs of fatigue or incipient failure.

Summary of Total Heart Replacement Experiment No. 6 (TH73C43B40AEC6, November 26, 1973):

Experiment No. 6 was a sterile, short-term evaluation with the purpose of determining the smallest experimental calf whose chest cavity would accommodate the AEC blood pump with an external electric motor.

Previous animal experiments were carried out using 110 to 123 kg calves. It was the purpose of this experiment, in addition to gaining surgical experience in implanting the AEC blood pump, to determine the minimum weight of calves that could be successfully implanted with the AEC blood pump.

Surgery was performed on a 93 kg male Holstein calf. No preoperative antibiotics were administered. Bjork-Shiley 29 mm inflow valves and 27 mm outflow valves were sealed into the fibrilized Silastic ventricles and the entire blood pump was autoclaved prior to surgery. An external electric motor was used to drive the blood pump at 120 beats per minute. A sternal split surgical procedure was used with the animal on bypass for 136 minutes. The animal was induced with Brevane followed by Halothane as an anesthesia.

Surgical Procedure:

After atrial cuffs and great vessel grafts were sutured in place and the blood pump inserted and connected, the chest cavity was closed. Aortic outflow and venous inflow pressures indicated that there was severe kinking of the pulmonary artery against the chest wall. Several attempts were made to manipulate the blood pump and grafts to reduce kinking. However, during all attempts to close the chest, the outflow pressures were reduced, due to kinking of inflow lines (venous and pulmonary). This experiment demonstrated that the use of the AEC blood pump should be restricted to calves with weight greater than 100 kg and adequate thoracic volume. From this and other past experiments it was determined that the calf weight of choice is 105 to 110 kg.

Summary of Total Heart Replacement Experiment No. 7 (TH73C46B43AEC7, December 11, 1973):

Experiment No. 7 was designed as a sterile long term evaluation of the pumping performance of the AEC blood pump using an external electric motor. From the previous experiments it was determined that an ideal experimental calf size would be 105 to 110 kg.

Surgical Procedure:

A sternal split surgical procedure was performed on a 107.5 kg male Holstein calf. Anesthesia was Brevane followed by Halothane. Silastic ventricles with fibrilized surfaces were used with Bjork-Shiley 29 mm inflow valves and 27 mm outflow valves. Ventricles and blood pump were autoclaved prior to surgery and the flexible drive shaft and casing were gas sterilized. Surgery required 3½ hours with the calf on heart-lung bypass for 130 minutes. Preoperative pulmonary function tests indicated adequate functional residual capacity of the calf's lungs. Recording equipment was adjusted to record venous and aortic pressures as well as pump r.p.m. and motor torque.

Postoperative Results:

The calf was taken off heart-lung bypass and the circulation totally supported with the AEC blood pump at 3½ hours after surgery started. Pulmonary tidal volume was excellent with mechanical ventilation support using 100% oxygen. Nine hours postoperative the animal's temperature was normal and was supported by 40% oxygen with a mechanical respirator. Cardiac pressures were excellent, venous filling pressure was 20 mm Hg and aortic outflow pressures were 125/75 mm Hg. Chest drainage had decreased, and tidal volume stabilized at 2000 cc. Blood gases were normal and the calf attempted to stand every 10 to 20 minutes. The external electric motor speed was steady at 900 r.p.m. with an average output torque of 0.6 in. lbs. and pump vacuum maintained constant at 5 in Hg. At 25 hours postoperative, the flexible drive shaft broke. There was no increase in torque noted at failure. The animal was quiet with little body movement. The shaft broke approximately two inches from the blood pump end. This coincided with the point where the shaft exited the chest wall.

Autopsy Results:

Autopsy of the calf revealed kinking of the aorta and pulmonary artery graphs and moderate compression of left atria. No kinking of the superior and inferior vena cava was observed. The thorax contained approximately 100 ml of unclotted blood and 400 ml of clotted blood. The lungs were excellent with no atelectasis or consolidation apparent. A large amount of ascite 6 liters was present, but the ascites was yellow in color with no blood present. Severe edema of the anterior mesentary was observed and the liver was congested and blood filled. The general appearance of the kidneys was good with only a few old infarcts.

The pusher cups of the AEC blood pump were free with no apparent sign of pump malfunction. The break in the drive shaft occurred quickly with a clean break. Worn portions of the flexible shaft were noticed on both ends of the shaft at approximately two inches from either end. There was a general lack of lubrication on the surface of the drive shaft. The lubricant had most likely worked its way into the core of the shaft. Upon careful inspection there was no evidence of shaft corrosion. Torque and speed measurements were recorded and values were obtained from the tracings just prior to the shaft breaking. As was deduced from the record tracing, there was no increase in torque

or decrease in motor speed that might be indicative of blood pump malfunction. Death was due to failure of the drive shaft. The physiological condition of the calf prior to termination was such that the animal could have probably survived at least 100 hours.

Summary of Total Heart Replacement Experiment No. 8 (TH74C2B2AEC8, January 10, 1974):

Experiment No. 8 was designed as a sterile, short term experiment to evaluate and confirm the surgical protocol for internally implanting a small electric motor and flexible drive shaft to power the AEC blood pump. See Figure XI-1 for an illustration of the implanted assembly.

Surgical Procedure:

The surgical procedure was similar to that used in Experiments No. 6 and 7 except a slightly heavier than normal calf was used (120 kg male Holstein). Silastic ventricles with fibrilized surfaces and Bjork-Shiley valves were implanted. Preoperative pulmonary function tests indicated that the calf's lungs were within normal limits. Recording equipment was set up to measure both venous and aortic pressures together with motor speed and torque.

Results of Experiment:

The electric motor was implanted to the right of the mid-line, subperitoneally near the costal arch anteriorly. See Figure XI-2 for surgical field view. A short eight inch flexible drive shaft was tunneled under the diaphragm from the chest cavity to the abdomen. The drive shaft was connected first to the blood pump and then to the electric motor. Difficulty in connecting the quick-connect atrial graft and great vessel connectors to the blood pump ventricle arose. Great force was needed to facilitate closing the quick-connects. This caused the ventricle to rupture at the quick-connect junction. Several attempts to repair the ventricles proved useless. However, the experiment was continued to evaluate the anatomical fit of the implanted electric motor.

The electric motor and short eight inch flexible drive shaft system was well accommodated in the calf's abdomen. The electric connections were tunneled under the calf's skin and exited from the animal's right side. The electric motor was started and the blood pump was allowed to pump blood. There was very little vibration or motion observed in the flexible drive shaft. Upon closing the muscle tissue and skin over the electric motor, it was noted that a shorter (6 inch) flexible drive shaft would be better suited for this internal electric motor implantation procedure.

Analysis of the bonding of the flexible drive shaft confirmed our cadaver fit trial experiments. An eight to ten inch bend radius was deemed to be the minimum bending expected during the course of the experiment. Photographic evidence of the electric motor and flexible drive shaft positions were made and the animal was terminated.

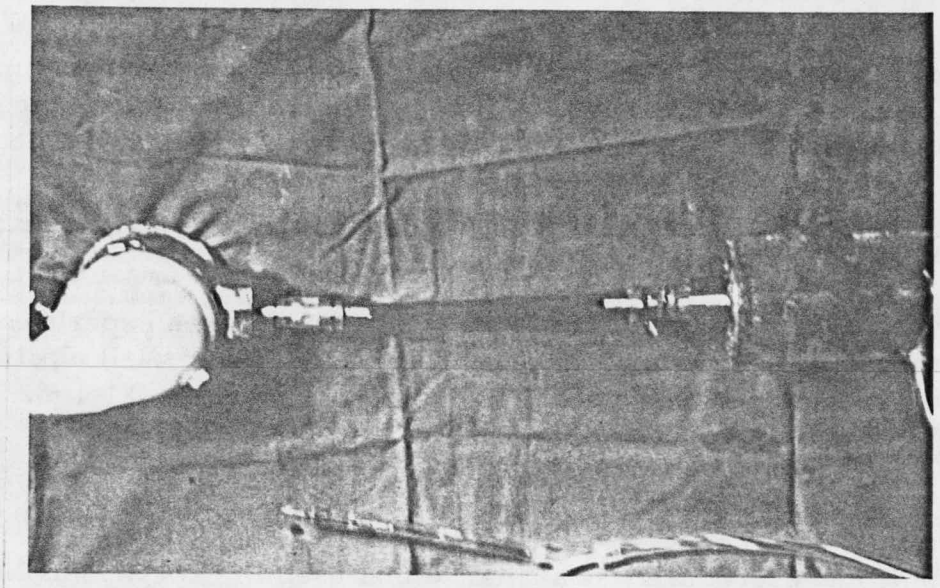


FIG. XI-1: Implantable electric motor, flexible drive shaft and blood pump assembly as it would appear in the experimental animal.

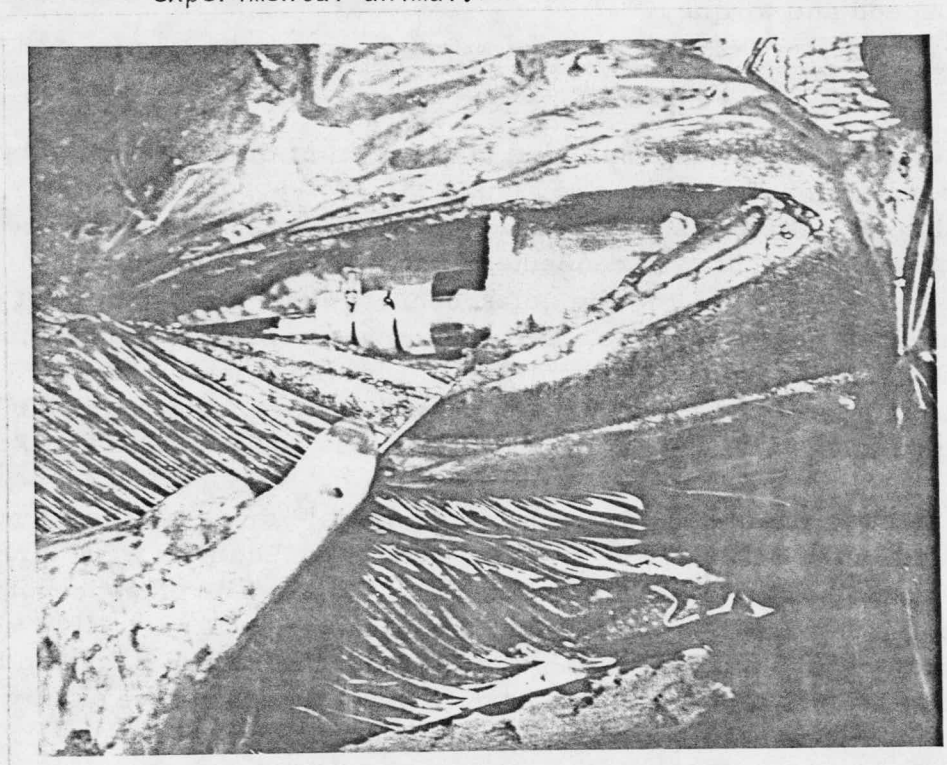


FIG. XI-2: Electric motor and flexible drive shaft implanted in abdomen prior to suturing overlying tissue.

Evaluation of the findings indicate that a small electric motor can be easily installed in the calf abdomen and that a short six to eight inch flexible drive shaft can be tunneled from the chest cavity into the abdomen with very little bending produced in the drive shaft. Problems encountered with the ventricle quick-connect junction dictated that a stronger rigid ventricle junction is necessary to adequately secure the quick-connect rings (female portions) to the AEC blood pump ventricles.

Summary of Total Heart Replacement Experiment No. 9 (TH74C9B9AEC9, February 14, 1974):

Experiment No. 9 was planned as a sterile long-term evaluation of the internally placed electric motor and flexible drive shaft to drive the AEC blood pump.

Surgical Procedure:

A sternal split surgical procedure was performed on a male Hereford calf weighing 105 kg. Anesthesia was Brevane followed by Halothane. Preoperative lung function measurements were within normal limits. Blood pump ventricles were constructed of Silastic rubber and all blood contacting surfaces were coated with fibrils. Ventricles and blood pump were autoclaved prior to surgery. Bjork-Shiley heart valves were glow discharged prior to insertion into the ventricles. The flexible drive shaft and electric motor were gas sterilized 72 hours and the calf was on heart-lung bypass for 120 minutes. Recording equipment was set up to record central venous and aortic pressure as well as electric motor r.p.m.

Postoperative Results:

As the calf was taken off heart-lung bypass and onto total support with the AEC blood pump, the electric motor controller stopped. Due to temporary pulmonary hypertension, very high aortic pressures on the order of 210/90 mm Hg were observed. By reducing the calf's blood volume, blood pressures were returned to normal physiological limits (150/90 mm Hg). Shutdown of the electric motor lasted approximately 1½ minutes, during which time circulation was aided by the heart-lung machine. One hour after surgery the calf was on mechanical breathing support with 40% oxygen, with a tidal volume of 2,200 cc. Atrial pressures were 145/90 mm Hg with 3 mm Hg central venous pressure. Chest drainage was minimal.

At ten hours postoperative the calf was still on 40% oxygen with mechanical ventilation. Atrial pressures were excellent (135/75 mm Hg), with mean central venous pressure (CVP) of 8 mm Hg. The electric motor temperature had increased to 44° C. Fluctuations in motor temperature from 43° C to 48° C were observed and were most likely due to movement of the temperature probe located near the internal electric motor. At 19 hours the animal stood for approximately two minutes. After 20 hours postoperative the motor controller overheated and once again stopped. Average torque measurements made during this incident were 7 to 11 oz. in. Since the motor is rated at 10 oz. in. the motor was being operated near peak capacity. The controller is built to trip if an electric current responds to an average torque of 13 oz. in. The controller

was off for approximately two minutes, after which the thermal relay device cooled sufficiently to allow the controller to operate again. A backup controller system was placed on standby at this time.

At 25 hours the animal again stood for a few minutes, chest drainage had stopped and the animal's reflexes were good. Motor temperature was 45° C. At 30 hours the animal was extubated and placed on 70% oxygen with a face mask. The animal once again stood. Atrial pressures were 125/80 with a mean CVP of 8 mm Hg. Respiratory rate was normal at 30 breaths/min. At 35 hours postoperative the animal was doing very well using a face mask with 70% oxygen. Respiratory rate was 33 per minute. Atrial pressures of 125/80 and a mean CVP pressure of 8 mm Hg were observed. At 35 hours and 20 minutes the calf attempted to stand and fell forward out of the cage. Two minutes later the animal was returned into the cage with no apparent damage other than one chest tube pulled out. At approximately 36 hours the motor controller again tripped by the thermal breaker. The backup controller was connected to the electric motor but it too tripped. Switching back and forth from one control unit to another for several minutes failed to maintain the blood pump operating. Vacuum readings indicated that the blood pump vacuum was being maintained at 5 in. Hg. Torque reading were off scale (greater than 15 oz. in.) while r.p.m. was low (approximately 200 to 300 r.p.m.). After five minutes of attempting to maintain operation of the blood pump and electric motor, the r.p.m. suddenly returned to normal (900 r.p.m.) and the torque lowered to three oz. in. The flexible shaft had broken terminating the experiment. See Figures XI-3 and XI-4.

Autopsy Results:

Upon autopsy of the calf no kinking of the aorta or compression of the left and right atria was seen. There was approximately 30% kinking of the pulmonary artery. General appearance of the thorax showed only small amounts of free and clotted blood. Ventral atelectasis was present in both the right and left lungs. No ascites was present in the abdomen. The external appearance of the liver indicated a small degree of swelling, but the liver appeared smooth. Both kidneys showed no signs of infarcts. The spleen, intestines, bladder and brain all appeared in excellent condition.

Tissue in the vicinity of the electric motor metal end plates showed signs of severe thermal damage. A large hematoma was present around the electric motor, probably resulting from suturing in the electric motor before anticoagulants had taken effect. Autopsy revealed that the electric motor temperature probe was approximately 2 cm from the read motor end plate. The thermal heat flux dissipated from the electric motor to the calf's body was estimated at approximately 10 watts. Most of this 10 watts was discharged through the end plates attached to the electric motor. Because of the small surface area of the end plates high heat flux existed (heat per unit area) and some tissue damage resulted.

Results of Experiment No. 9 demonstrated that with a calf of suitable size and with proper reinforcement of the blood quick-connect rings, an electric motor can be used to simulate the thermal converter in driving the blood pump. Complete implantation of the electric motor seemed well tolerated by the calf and if high heat flux as can be eliminated there should be minimal trauma due to implanting and maintaining the electric motor within the abdomen.

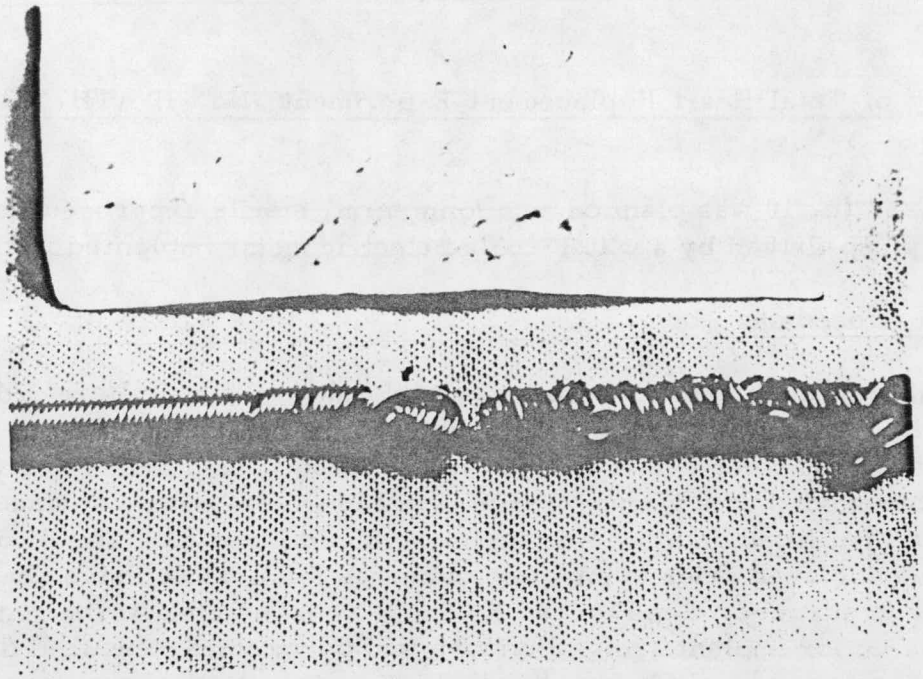


FIG. XI-3: Detailed view of the point of failure of the flexible drive shaft.

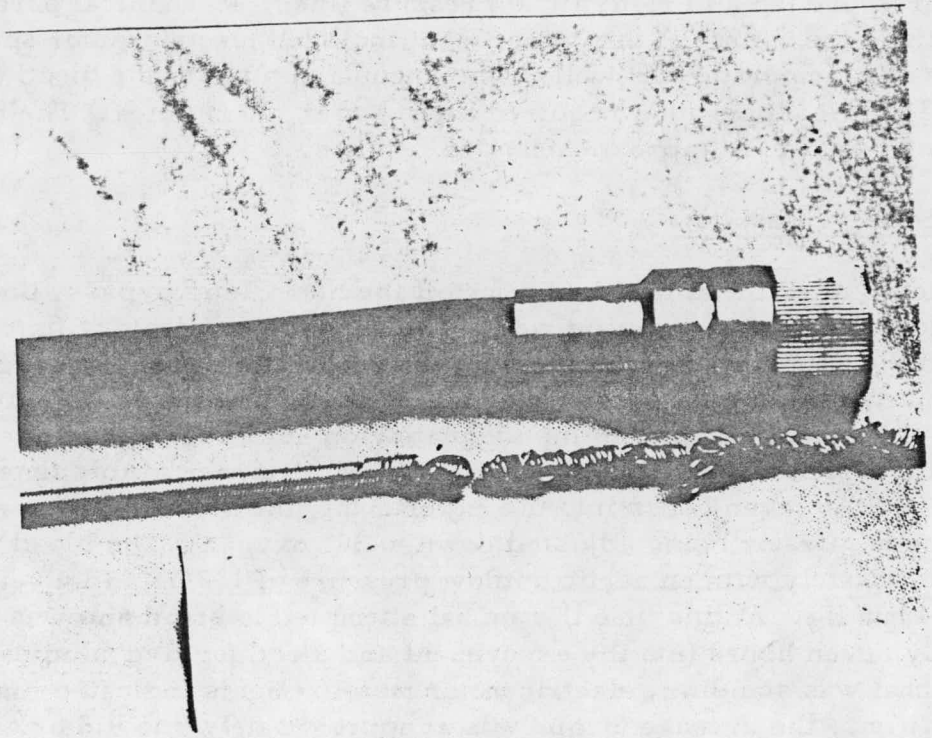


FIG. XI-4: View showing point of failure of drive shaft relative to position in shaft housing.

Summary of Total Heart Replacement Experiment No. 10 (TH74C21D21AEC10, May 29, 1974):

Experiment No. 10 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.

Surgical Procedure:

A sternal split surgical procedure was performed on a male Hereford, approximately 102 kg in weight. Anesthesia was Brevane followed by Halothane. Preoperative lung function measurements were within normal limits. Blood pump ventricles were constructed of Silastic rubber coated with Dacron fibrils on all blood contacting surfaces. These ventricles were then fitted onto the Westinghouse Blood Pump #3. The blood pump with ventricles was autoclaved prior to surgery, whereas the flexible drive shaft was gas sterilized prior to surgery. See Figures XI-5 and XI-6 for view of the motor and shaft assembly prepared for implantation. Physiological parameters measured during the course of this experiment included aortic pressure, central venous pressure, right and left atrial pressures, and pulmonary arterial pressure. Aortic pressure and central venous pressure lines were removed after 24 hours and replaced with their respective atrial graft pressure tap and right atrial pressure lines. Mechanical parameters measured during the course of this experiment included electric motor speed, electric motor torque and temperature as well as the vacuum applied to the blood pump mechanism. The complete surgical operation required three hours, 40 minutes. The calf was on the heart-lung bypass for approximately 135 minutes.

Postoperative Results:

Two hours after the animal had come off the heart-lung bypass, the electric motor and blood pump were running well. The animal's respiratory functions were adequate and the animal was breathing with the respirator set at 50% oxygen. The blood pump was maintaining a good pressure of 120/80 aortic pressure. At four hours into the experiment, the animal was breathing adequately on 40% oxygen, again maintaining adequate outflow pressures of 125/90 mm Hg. Chest drainage at this time had accumulated to about 600 ml. At seven hours into the experiment, the animal was breathing still very well, with the respirator being adjusted down to 30% oxygen. The blood pressures were maintained adequately with an aortic outflow pressure of 130/75 and a venous filling pressure of 4 mm Hg. At this time the animal attempted to stand and was up at approximately seven hours into the experiment and stood for five minutes unassisted. While the animal was standing, electric motor measurements indicated that the speed was at 900 r.p.m., the average torque was at approximately 9 to 9.5 oz. in. while a normal motor temperature of 39.5° C and 5 in. of mercury was being maintained on the blood pump. At nine hours into the experiment, the animal was still breathing well on 30% oxygen, and excellent blood pressures were maintained at 135/80 mm Hg aortic outflow with a -2 mm Hg venous filling pressure. Again the animal attempted to stand. At 10 hours into the experiment the chest drainage had increased. This was to be expected with the increased movements of the calf and his many attempts to stand. The

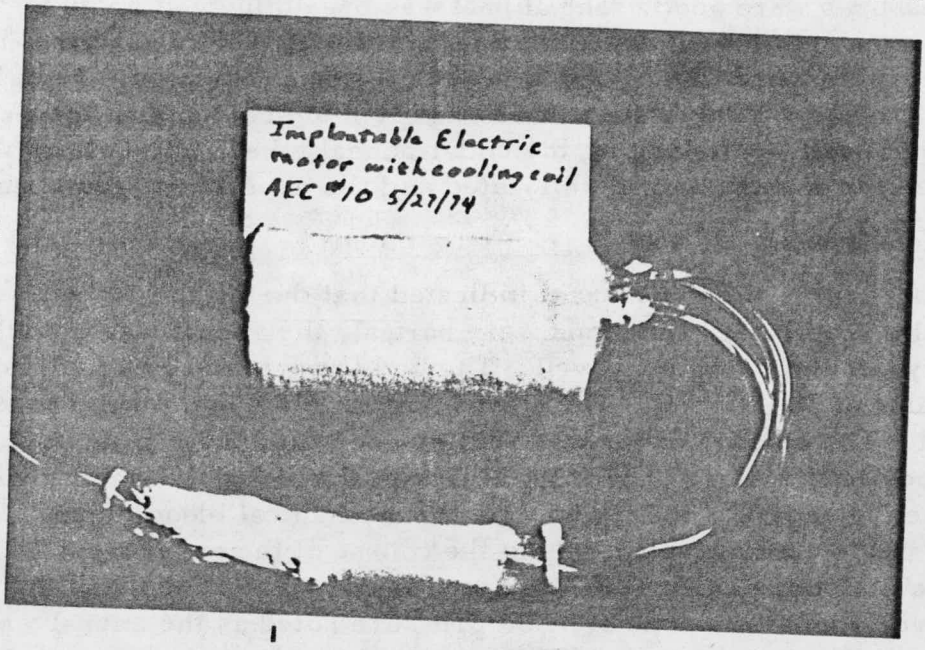


FIGURE XI-5

Electric motor has been wraped with a copper cooling coil and the entire motor assembly covered with Dacron cloth to ensure tissue ingrowth and fixation after implantation. Motor is gas sterilized 72 hours prior to surgical implantation.

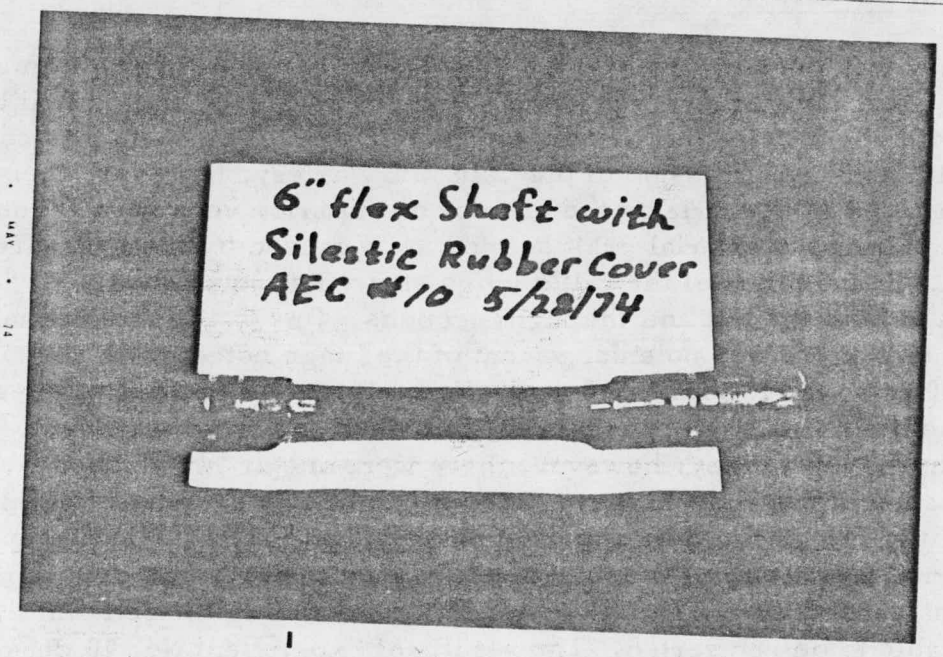


FIGURE XI-6

Flexible Drive Shaft - Neoprene casing with Phosphor bronze liner and 1/8" diameter core. Assembly is covered with Silastic rubber to protect drive shaft. Shown here prior to surgery. Shaft is gas sterilized 72 hours before surgery.

chest drainage had increased to approximately 1700 cc. At 12 hours into the experiment, the animal was becoming restless, attempting to stand off and on every 20 to 25 minutes. Blood pressures were good. The animal was breathing well on 30 to 35% oxygen. The animal was maintaining an excellent tidal volume of 1800 cc -at normal body temperature. Blood pressures were 130/75 with a venous filling pressure of -3 mm Hg. During the 14th hour postoperatively, the animal attempted to stand and in the process accidentally extubated himself by dislodging the endotracheal tube. Efforts to replace this tube proved useless and the animal suffocated and the experiment was terminated at approximately 14 hours.

In summary, the experiment indicated that during the 14 hours postoperatively, the animal's respiratory functions were normal, the animal was quickly adjusted to 30-35% oxygen and doing very well. The body temperature had adjusted itself to a normal value of 38-38.5^{O} C. The electric motor and blood pump systems seemed to work well. The electric motor was kept at a constant 900 r.p.m. and maintained at a normal body temperature of 39 - 39.5^{O} C with the aid of the water cooling system. The vacuum held steady at 5 in. Hg hold on the mechanical blood pump. There was no variation in the vacuum noted during the course of the experiment. The blood pump system maintained adequate blood pressures during the course of the experiment with no large variations in torque of blood pressure noted as the animal was in a resting position or as the animal attempted to stand. The blood pressures varied from a high of 135/80 to a low of 120/80 during the course of the experiment. Filling pressures varied from a +2 to a -5 mm Hg measured at the right atrial pressure tap. The projected experimental outcome was excellent since the animal was up at approximately seven hours in this experiment. The experimental animal recuperated very quickly from surgery, and had the calf not accidentally extubated itself at 14 hours, the animal possibly could have survived for a much longer period of time.

Autopsy Results:

Autopsy was performed while the calf was in an extended position and upon opening the chest cavity there was noted about 400 ml of free and clotted blood on the right side with about twice this amount on the left side. The aorta was compressed about 20% with some compression of the pulmonary artery; however, there was no compression noted in the atria or the inferior or superior vena cava. The kinking noted in the pulmonary arterial graft seemed to be caused by the pressure tap built into the PA graft. Examination of the calf's lungs showed some actelectasis with some compression to both the left and the right sections. Due to the short term nature of this experiment, there was no enlargement of the lungs noted, with the right lung weighing 640 gms, the left lung 540 gms. No ascites were noticed in the abdomen; however, the liver was slightly enlarged, but was good on appearance. There were no infarcts in the left kidney; however, there were one or two small infarcts on the posterior section of the right kidney. The spleen had an excellent external appearance with a weight of 180 gms and no apparent enlargement. The intestines appeared good as did the internal mesentery of the intestines. Cause of death was determined to be suffocation as caused by the animal accidentally extubating himself and the endotracheal tube was unable to be reinserted. The results of Experiment No. 10 demonstrated adequately that a calf of a little over 100 kg can be maintained with the AEC blood pump

being driven by an electric motor. The addition of the water-cooled coil wrapped around the electric motor seemed to adequately dissipate heat from the electric motor and we were able to maintain the electric motor at normal body temperature during the course of the experiment. The addition of the cooling coil seemed to impose no problem in implanting the electric motor to power the AEC blood pump. Complete implantation of the electric motor and the electric motor cooling coil seemed to be easily tolerated by the calf and had the calf been less active and not extubated himself accidentally, this experiment could have lasted for a much longer period of time.

Summary of Total Heart Replacement Experiment No. 11 (TH74C22D22AEC11 June 10, 1974):

Experiment No. 11 was designed as a long-term, sterile experiment to evaluate the AEC blood pump driven by a water-cooled electric motor implanted in the abdomen and coupled to the blood pump by a short 6" flexible drive shaft.

Surgical Procedure:

A sternal split procedure was performed on a 103 kg Holstein calf. The implanted blood pump consisted of a Westinghouse Blood Pump mechanism, #3, fitted with Silastic ventricles, and surfaces coated with Dacron fibrils. The ventricles were fitted with four Bjork-Shiley inflow and outflow valves. The complete blood pump was autoclaved prior to surgery. Preoperative screening pulmonary tests were performed on the calf and indicated that the lungs were normal. Recording equipment was set up to monitor physiological parameters of the calf and mechanical parameters of the cooling system and electric motor. Pressure taps were provided in the pump to monitor the right and left atrial pressure, the pulmonary arterial pressure and the aortic pressure. A central venous pressure line and aortic pressure line were inserted during surgery but were removed 24 hours postoperatively. Mechanical characteristics of the system monitored continuously included speed of the electric motor, motor torque, vacuum maintained on the blood pump and the motor temperature.

The animal was induced initially with Brevane and maintained with Fluothane. Surgery required about five hours with the calf on the heart-lung bypass for three hours and 25 minutes.

Postoperative Results:

At two hours after surgery, the animal was breathing regularly with respiratory assistance @ 40% oxygen. Blood pressures were adequate with aortic pressures of 120/105 mm Hg and a venous filling pressure of 2.5 mm Hg. Motor temperature was approximately equal to body temperature. Vacuum was stable at five in. Hg, on the blood pump. The average motor torque was approximately nine oz. in. At seven hours into the experiment, the pulmonary tidal volume of the calf had leveled off at approximately 1500 cc. The animal was continued on the Bird respirator with 40% oxygen, maintaining blood pressures of 140/105 mm Hg outflow pressure with a filling pressure of seven

mm Hg. The electric motor had now equilibrated with body temperature and reached 38.5° C. Average motor torque had increased to approximately 10 oz. in. The vacuum was steady at five in. Hg. At 10 hours into the experiment, pulmonary tidal volume had increased to 150/115 with a filling pressure of six mm Hg measured at the right atrial cuff pressure tap. From 11 to 20 hours postoperatively, the animal was maintained on mechanical respiratory assistance at 40% oxygen. Tidal volume held steady at 2200 cc. The body temperature fluctuated from 37 to 36.5° C. The electric motor and drive mechanism seemed to perform adequately with an average torque of nine to ten oz. in. at a motor speed of 900 r.p.m. Vacuum was maintained steady at five in. Hg. The blood pressure varied from 130/100 mm Hg to 127/87 mm Hg. Right atrial pressure varied from a low of three mm Hg to a high of seven mm Hg. Chest drainage had stopped at approximately 18 hours after an accumulation of 1450 cc of chest fluid. Some fluid drained from the motor incision in the abdomen but stopped at approximately 850 cc. During this 10 hour period, one liter of blood was transfused in the calf. From 21-30 hours postoperatively, the animal was maintained on mechanical respiratory assistance with 40% oxygen. Tidal volume was consistently measured at 2,000 cc with the body temperature steady at 38° C. The mechanical drive system worked well during this period of time. Motor speed was 900 r.p.m., the average torque 9-10 oz. in. Vacuum was steady at five in. Hg with the mean aortic blood pressure of the pump 105 mm Hg with a filling pressure of 8-8.5 mm Hg. The reflexes of the animal were minimal with only some eye movement noted. The animal did not attempt to stand. From 31-40 hours postoperatively, mechanical breathing assistance was maintained at 40% oxygen. Tidal volume remained unchanged at 2000 cc. The body temperature had decreased to approximately 37.5° C. Mechanical drive system was maintained at 900 r.p.m.; however, average motor torque had lowered to approximately eight oz. in. while the venous filling pressure remained at 5-7 mm Hg. The aortic outflow pressure decreased to an average of 70 mm Hg, with a systolic/diastolic reading of 80/60. Reflexes were very poor during this 10-hour period of time. Breathing became very shallow. Heat lamps were placed over the animal in an effort to increase his body temperature, but these proved ineffective. At 41 hours into the experiment, the animal was still maintained by mechanical respiratory assistance on 40% oxygen. Blood gases were normal. Body temperature had now lowered to 38° F with the tidal volume at 1800 cc. Blood pressures were 90/65 with a filling pressure of five mm Hg. Motor temperature had also lowered along with the average torque value to 7.5 oz. in. The animal's reflexes were very poor and it appeared as though the animal had suffered some brain damage, possibly due to the lengthy surgery and the 3½ hour heart-lung bypass time required. At 43 hours into the experiment, the animal still had very poor reflexes. Many physiological parameters were normal with the animal breathing 40% oxygen. Blood pressures were steady at 92/68 mm Hg with an average filling pressure of six mm Hg. At this time it was determined to discontinue the experiment. There appeared to be no improvement seen in the animal's condition so the experiment was terminated at approximately 43 hours 30 minutes post-operatively. However, the blood pump appeared to maintain the circulatory assistance and maintained a normal physiological condition.

Autopsy Report:

The autopsy was performed with the animal in a suspended position using bone pins. The sternum was tightly colsed with wire sutures maintaining good closure.

There was both free and clotted blood present in the chest with approximately 1300 cc in the right side of the chest and 320 cc on the left side of the chest. There was no kinking evident of the aorta or of the pulmonary artery. The right atrium was somewhat posterior and rotated. The bend radius of the flexible drive shaft appeared to be about six inches with no sharp kinking noted. No compression of the atria was noted, nor was there any compression of the superior or inferior vena cava. Upon examination of the blood pump, the right inflow quick connect appeared not to be completely closed, which may have been a source of bleeding. A small clot was found around the inflow valve at the juncture between the valve and the pulmonary vein graft. The left ventricle appeared very clean with no problems noted on the inflow or the outflow quick connect and the valve was very clean. There was some actelectasis noted on the lower tip of the left lung while the right lung had complete actelectasis evident over the entire lung. There was a small ascites volume of approximately 450 ml noted in the abdomen. There was, however, no edema of the interior mesentery evident. The liver appeared good. Kidneys appeared in excellent condition with only a few small infarcts in the left kidney. The spleen, intestines, and bladder all appeared normal. Sections of the brain were collected and sent to the histopathology lab for analysis. Upon visual examination of the brain section, no clots were seen. Histopathology results of the brain showed sections of the cerebellum with spongenosis of both the grey and white matter, indicating possible cellular edema. Some focal paravascular hemorrhages were also noted in this particular segment. These changes in the brain are suggestive of abnormal pressures resulting in inefficient fluid outflow as well as vascular hemorrhages which could have resulted in the animal's comatose condition.

During the autopsy, the flexible drive shaft appeared initially to have a general curvature of about six inches in bend radius. Upon closer examination, there was found a sharp dent of approximately 30-35^{O} occurring approximately two inches from the blood pump and of the flexible drive shaft coupling. Please refer to the accompanying photographs (Figures XI-7 and XI-8).

Summary of Total Heart Replacement Experiment No. 12 (TH74C28D28AEC12, July 30, 1974):

Experiment No. 12 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. The flexible drive shaft used in this particular experiment was similar to previous six-inch flexible drive shafts except with the addition of a reinforced drive shaft casing that would hopefully eliminate any sharp kinking or bending in the shaft casing. A sternal split surgical procedure was performed on a 105 kg Holstein calf. AEC Blood Pump #3 was used with Silastic ventricles coated with Dacron fibrils. The internal electric motor was water cooled and anesthesia employed was Brevane followed by Fluothane. Physiological parameters measured during this experiment included aortic pressure, central venous pressure, right and left atrial pressure, and pulmonary arterial pressure. Aortic and central venous pressure lines were removed after 24 hours. Mechanical characteristics of the driving system monitored included r.p.m., electric motor torque, motor temperature, and vacuum maintained on the mechanical blood pump. Preoperative screening pulmonary tests were performed on the calf and

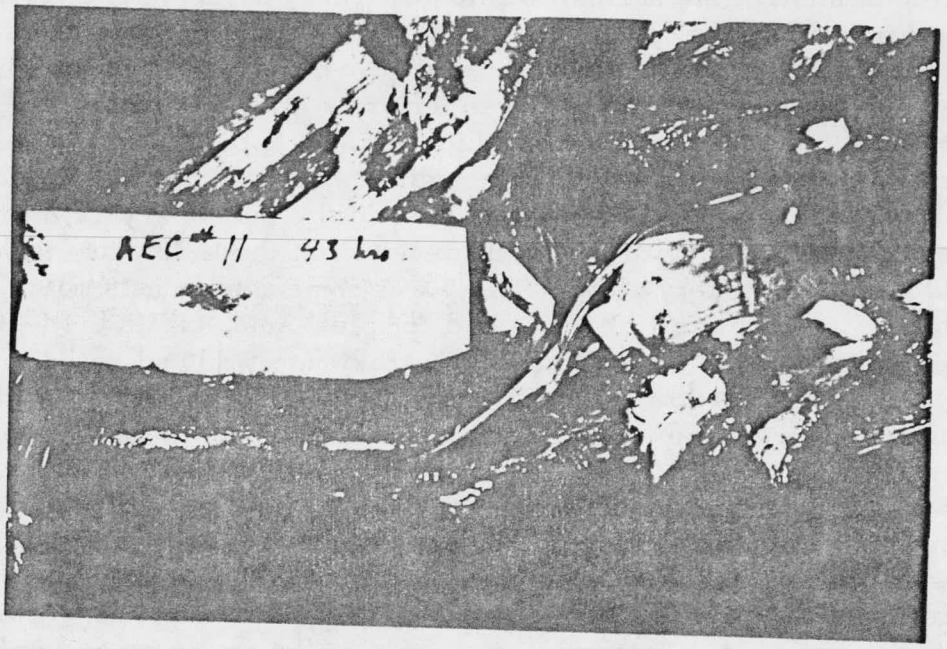


FIGURE XI-7

Autopsy photo illustrating the bending of the unreinforced flexible drive shaft casing used in Experiment AEC #11

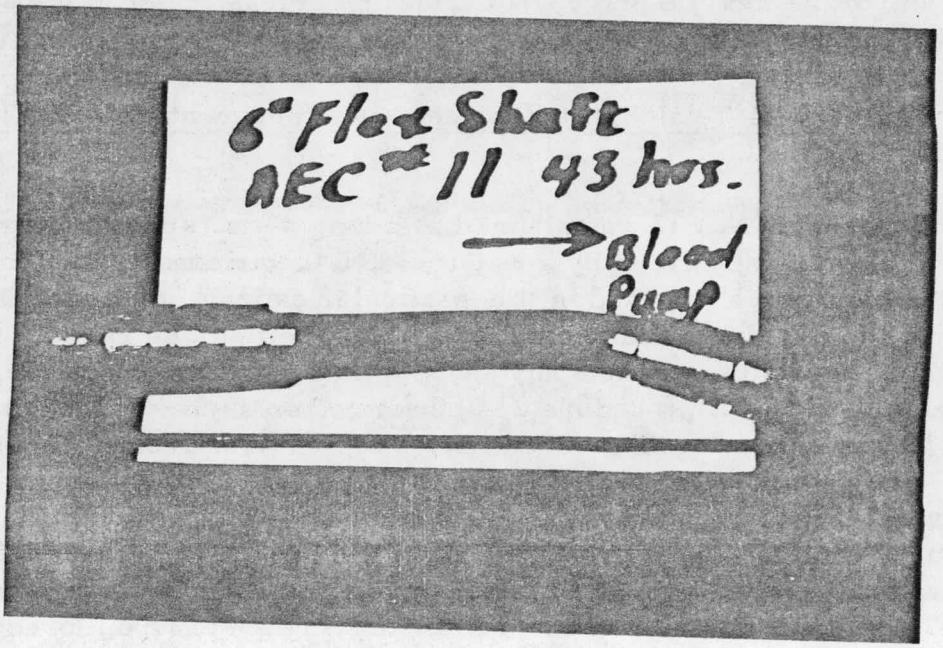


FIGURE XI-8

Illustrated here is the amount of residual bending after the 43 hour implantation of the flexible drive shaft.

the calf's lungs appeared normal. The AEC blood pump and ventricle system was autoclaved prior to surgery. The electric motor system and flexible drive shaft coupling components were gas sterilized 72 hours prior to implantation. Total surgical time was approximately three hours. The reason for the long bypass time was due to a leak in one of the quick connects. This had to be rectified before the chest could be sutured closed, resulting in the animal being kept on partial bypass for a long period of time.

Postoperative Results:

At three hours into the experiment after surgery, the animal was maintained with mechanical breathing assistance on 50% oxygen. Tidal volume was 2100 cc. The body temperature was approximately 34 ^{O} C. The mechanical driving system was running at 900 r.p.m. with an average torque of 6.5 to 7 oz. in. recorded. The cooling coil maintained the electric motor temperature at 35.8 ^{O}C. Average aortic pressure of 120 mm Hg was monitored with a filling pressure of six mm Hg. At six hours into the experiment, the animal was still being maintained with respiratory assistance. The calf showed some erratic movement and the reflexes were only slight. Mechanical drive system functioned satisfactorily. The motor temperature was 38^{O} C. Systolic/diastolic pressures were 100/35 mm Hg with a venous filling pressure of 12 mm Hg. Chest drainage had increased to approximately 3300 ml. At nine hours postoperatively, the animal showed signs of severe convulsions with only slight reflexes. Ambutal and Curare were given as a sedative to quiet the animal down. Adequate blood pressures were maintained with the drive system, aortic pressures were 130/70, with a filling pressure of 22 mm Hg. At 23 hours into the experiment, the animal was still being maintained with respiratory assistance on 60% oxygen. Tidal volume was 2500 cc. Blood gases were normal and other physiological parameters were normal. The electric motor was running normally with a nine oz. in. average torque. The motor's temperature was at body temperature. The vacuum maintained on the blood pump was steady at five in. Hg. Aortic pressures were 105/45 mm Hg with a filling pressure of 18 mm Hg. With the animal still in a comatose condition showing no signs of improvement, it was decided to end the experiment at 23 hours postoperatively.

Autopsy and Summary of Experimental Results:

The autopsy on the calf was performed with the animal laid on its side rather than suspended. This would eliminate any bending in the flexible drive shaft coupling. Upon opening the left thorax, approximately 1000 cc of clotted blood was found with no free unclotted blood seen. There was very little blood in the right thorax. The blood pump was close against the calf's sternum with no kinking evident at the aorta or pulmonary artery. There was only mild compression of the atria with no compression seen in the superior or interior vena cava. The most significant finding was seen with the flexible drive shaft. Exposed, it revealed a smooth curvature of approximately 5-6 in. in bend radius with no kinks at either end of the flexible drive shaft casing (see Figure XI-9 and XI-10). Both the right and left ventricles appeared in excellent condition with no signs of leaking at the inflow or outflow quick connect sites. The right lung showed moderate actelectasis at the upper lobe with the left lung showing no

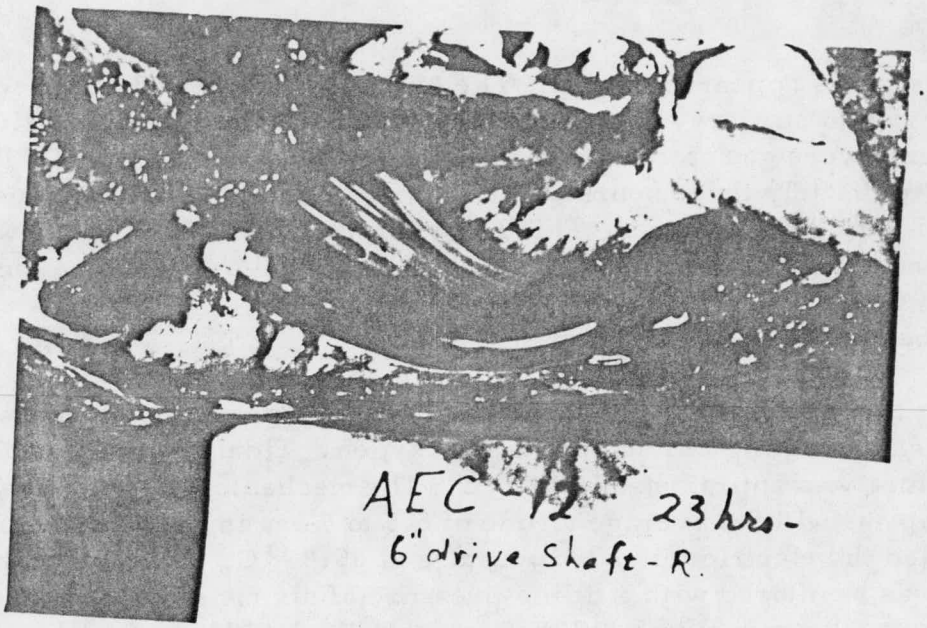


FIGURE XI-9

In contrast to Figure there is a gentle smooth curveture of this reinforced drive shaft casing used in experiment AEC #12

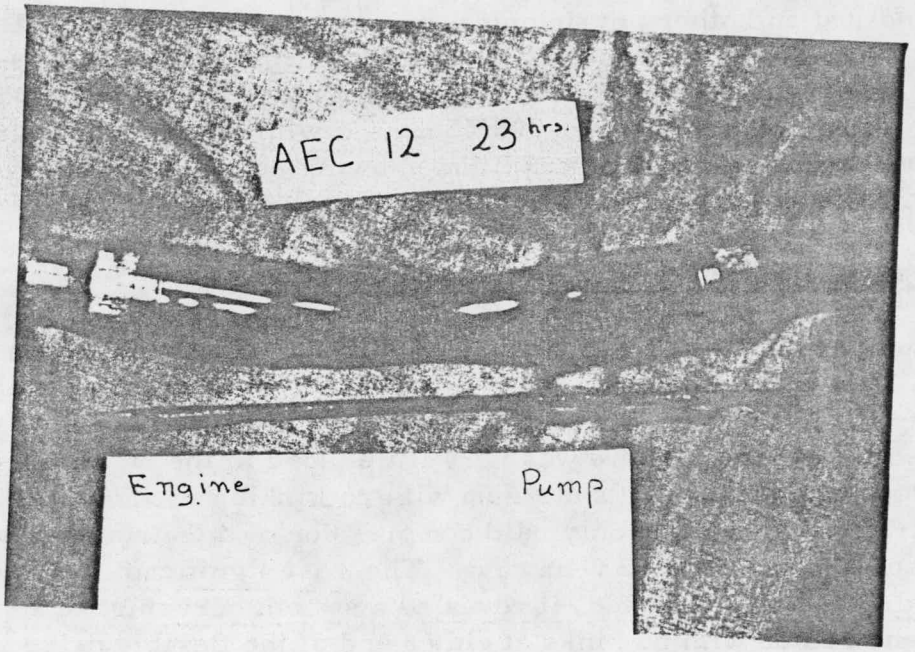


FIGURE XI-10

The casing reinforcement has eliminated the sharp bending from occuring at the two ends of the flexible drive shaft casing.

actelectasis or consolidation. Due to the short term nature of this experiment, there was no ascites seen in the abdomen and liver, kidneys, spleen and intestines all appeared normal. However, upon examination of the brain, there were signs of severe hemorrhaging in the spinal cord area. Sections were sent to a histopathology lab for analysis. Histopathology results on the brain scan showed numerous focal macrohemorrhages scattered throughout the brain stem with the hemorrhages most concentrated in the grey matter. There were 8-10 neurons in the lateral horn involved by the focal hemorrhagic processes. Other sections of the brain showed leukocytic margination in the the smaller vasculature of the brain. Some focal paravascular hemorrhages are also noted in this particular section.

Summary of Total Heart Replacement Experiment No. 13 (TH74C29D29AEC13, August 5, 1974):

Experiment No. 13 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. The flexible drive shaft coupling consisted of a thick neoprene reinforced drive shaft casing designed to prevent sharp bending in the drive shaft core.

Surgical Procedure:

A sternal split surgical procedure was performed on a Holstein calf approximately 101 kg in weight. AEC Blood Pump #3 was used; the Silastic ventricles coated with Dacron fibrils and fitted with Bjork-Shiley vitreous carbon heart valves. The blood pump mechanism and Silastic ventricles were autoclaved prior to surgery. The implantable electric motor and cooling system along with the flexible drive shaft coupling mechanism were gas sterilized 72 hours prior to surgery with ethylene oxide. The animal was anesthetized with Brevane followed with Fluothane. The surgery progressed with few problems until the AEC Blood Pump mechanism was inserted into the animal's chest and connected to the electric motor driving system. When the electric motor was turned on, the fuse of the motor controller blew, indicating a malfunction somewhere in the driving system. A second stand-by motor control system was connected to the electric motor. It also blew a fuse while attempting to power the artificial heart. The AEC Blood Pump was disconnected from the flexible drive shaft mechanism and the electric motor was run free. The motor operated normally, indicating that the problem was located in the AEC Blood Pump mechanism. The pusher cups of the AEC Blood Pump were free to move when pushed from one side to the other side. However, the AEC Blood Pump would jam at extreme left ventricular systole. With no back-up AEC Blood Pumps available the experiment was terminated at this point. The blood pump was cleaned and sent back to the Westinghouse laboratory for further examination.

Summary of Total Heart Replacement Experiment No. 14 (TH74C31D31ERDA, August 16, 1974):

This experiment was planned as a long-term sterile experiment to evaluate the ERDA Blood Pump driven by a water cooled electric motor with a reinforced flexible drive shaft and casing implanted in the abdomen of a calf.

Surgical Procedure:

A sternal split surgical procedure was performed on a Holstein calf approximately 110 kg in weight. ERDA Blood Pump No. 2 was used with Silastic pyrolytic carbon valves. The ERDA Blood Pump mechanism and Silastic ventricles were autoclaved prior to surgery. The implantable electric motor and cooling system, along with the flexible drive shaft coupling mechanism, were gas sterilized 72 hours prior to surgery with ethylene oxide. 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 pressure, right atrial pressure and pulmonary arterial pressure. Mechanical performance parameters measured were motor speed, torque, electric motor temperature and the vacuum maintained within the blood pump mechanism. The experimental animal had preoperative lung function which indicated normal breathing capacities. Heart-lung bypass time was approximately 133 minutes. Surgery required approximately 3½ hours.

Postoperative Recovery:

One hour into the experiment with the animal off the surgical table and into the postoperative cart, the average motor torque was nine oz.-inches and motor temperature was 40.5° C. Arterial blood pressure was adequate at 120/190 mm Hg and a filling pressure of approximately four mm Hg on the right ventricle and four mm Hg on the left ventricle. At seven hours into the experiment the average motor torque was 10 oz.-inches, motor temperature was 37.5 °C and aortic pressure was 120/75 mm Hg with an average filling pressure of five mm Hg in the left ventricle. At this time the animal attempted to stand and pulled out the power line which was immediately reconnected. At 10 hours into the experiment the animal was repositioned and a high torque on the electric motor was observed when the animal's right front shoulder was elevated. The average torque was 10.5 oz.-inches, with some high torque values at 12 to 12.5 oz.-inches. At 10 hours into the experiment 2600 cc of fluids had accumulated in the chest drainage bottle. Continually the animal attempted to stand. There appeared to be a profuse amount of thoracic bleeding at this time. In order to correct bleeding the animal was returned to the surgery table at 12 hours into the experiment and reopened. At 14 hours into the experiment the animal was off the surgery table. At 16 hours into the experiment (two hours after the second surgery) the calf began to awaken from the anesthesia and attempted to stand. The electrical connector connecting the electric motor speed controller with the electric motor began to operate intermittantly, resulting in frequent over-speeding of the electric motor. Occasionally the electric motor would stop. At 17 hours into the experiment the electric ventricle connector was resoldered and epoxied to eliminate this connector problem. At 20 hours into the experiment the aortic blood pressure was 120/100 with a filling pressure in the left ventricle of five mm Hg and six mm Hg on the right side of the blood pump.

Drainage from the chest drainage tubes was diminished with the second surgery, solving the bleeding problem that had been seen earlier in the experiment. At 32 hours into the experiment the fuse on the motor controller opened because of the high torque

condition and power to the blood pump was off for approximately four minutes. After replacing the fuse the electric motor speed was reduced to approximately 700 r.p.m. to reduce the torque load on the motor. High torques on the electric motor were noticed every time the animal changed his position or was moved. At 45 hours into the experiment the reflexes of the animal were fair with some eyelid movement. Again, slight movement of the animal would cause high torque conditions and blood pressures would also increase. The blood pump performance seemed to be somewhat position sensitive. At 58 hours into the experiment the animal appeared to be extremely constipated. There was some involuntary muscle spasm but the animal was unable to move. At 65 hours into the experiment adequate blood pressures and blood gases were maintained while the animal was on 40% oxygen with the Bird respirator. The aortic blood pressures were 110/75 with a filling pressure of approximately three mm Hg, with very high torques, 13.5 oz.-inches and greater. At 80 hours into the experiment reflexes were very poor although the animal's blood gases were maintained adequately on 60% oxygen with the Monoghan respirator. Aortic pressures were 110/80 mm Hg. At 87 hours it was decided that further postoperative care would no longer provide useful experimental data and the animal was terminated and an autopsy performed.

Autopsy Report:

Upon examining the artificial heart inside the chest cavity the relative position of the heart to the sternum was very good, with very little dead space between the flow port of the blood pump and the sternum. There was no kinking of the aorta or pulmonary artery evident and there was very little compression of the atria or the superior and inferior vena cava. Close examination of the quick connects revealed they were all tightly sealed with the exception of the pulmonary artery quick connect which appeared to be pulling out of the ventricle.

The animal appeared to be dehydrated. The right lung weighed approximately 910 gm, the left lung 700 gm. This totalled approximately 1600 gm which gave no indication of excessive weight of the lungs. The liver weighed 3100 gm which is greater than the 1.65% of body weight usually considered normal for these calves.

The kidneys did not appear to be enlarged. There were a few moderate infarcts in the left kidney and numerous small infarcts in the right kidney. Upon examination of the spleen there were some hemorrhages evident around the secum. Sections of the brain were sent for histopathology and the results were as follows: "Microscopic examination of three sections of the brain at various levels revealed some perivascular edema with rather severe edematous changes within the parenchyma of the brain. It does appear to be a focal area of corticomalacia, which may have resulted from being exposed to water during the removal process. There is also evidence of neurinal shrinking throughout the brain tissue. This is generalized and may be associated with anoxia to the brain. There are some layers within the brain which appear to be markedly congested."

Summary:

This experiment was successful in that the longest implant time to date had been achieved with a totally implantable electric motor and drive shaft. Difficulties arose

with the increased bleeding early in the experiment and the necessity of reopening the animal's chest to resolve bleeding problems which always cause a risk to the animal and the possibility of throwing emboli into the organs, especially the brain. However, the second surgical procedure did in fact stop the bleeding and the animal tolerated the second operation satisfactorily. The animal was perfused adequately and maintained blood pressures and blood gas values within normal limits. We did experience problems with high motor torques as the animal changed positions. This did provide us with experience as to what positions the animal could assume without overloading the flexible drive shaft. During one of these calf movements we did blow the fuse to the electrical controlling unit of the electric motor, but this was corrected with an insertion of a new fuse into the motor controller. In the latter half of the experiment, although bleeding was controlled, there was evidence of a comatose condition due to possible brain damage, probably sustained when power to the electric motor was interrupted for four minutes. This was not, perhaps, a fair test of the pumping capacity of the ERDA Blood Pump but it did in fact allow us to experiment with the animal in varying positions and to examine the high and low torque values produced from these position changes.

Cooling of the electric motor seemed adequate with the water cooling system maintained on the electric motor. There were no incidences of overheating. The animal was terminated at 87 hours since further postoperative care would not provide useful experimental data.

Summary of Total Heart Replacement Experiment No. 15 (TH74C41ERDA15, November 21, 1974):

Experiment ERDA15 was a long-term sterile experiment designed to evaluate the ERDA Blood Pump driven by a water-cooled electric motor implanted in the abdomen with a 3/16" drive shaft core and reinforced drive shaft casing.

Surgical Procedure:

A sternal split procedure was performed on a 98 kg male Holstein calf. The ventricles were fibrilized Silastic rubber, mounted on WANL Blood Pump No. 2 with polycarbonate quick connects. The driving system was an abdominally implanted, water-cooled electric motor. Anesthesia was Brevane induction followed by fluothane. Mechanical and physiological parameters measured during surgery included aortic pressure and central venous pressure. After surgery, continuous monitoring of aortic pressure, right atrial pressure, left atrial pressure and pulmonary arterial pressure was made. Mechanical parameters monitored included speed of the electric motor, motor torque, vacuum on the Blood Pump and electric motor temperature.

Preoperative pulmonary function tests performed on this calf yielded a functional residual capacity of 5,440 cc.

Surgery required approximately 3½ hours with the animal on heart-lung bypass for 140 minutes. The polycarbonate quick connects worked very well. There was no leaking apparent around the quick connects. During surgery, as preparations were

made to go off the heart-lung bypass, some foam appeared in the right ventricle and there appeared to be a source of air leaking into the blood stream. At this time it was decided to flood the chest with saline to prevent additional air leaking into the blood. This necessitated a rapid closure procedure that did not allow the surgeons time to isolate and stop several small sources of bleeding near the sternum incision.

Postoperative Results:

At six hours into the experiment the animal was able to stand with some assistance. The animal stood for four to five minutes. At this time there was a large amount of bleeding from the chest drainage tubes (approximately 2,000 cc total had been collected). At nine hours into the experiment the bleeding had not stopped so the animal was reopened to find and eliminate the source of bleeding. During this second surgical operation there were no specific sites located that could be associated with the excessive bleeding. However, it was found that some bleeding was occurring at the sternal split incision. Bleeding there was stopped and the animal was resutured. The second operation was completed at 10 hours into the experiment. During this operation blood handling components appeared to be functioning satisfactorily and there was no source of blood loss associated with the polycarbonate quick connects. Between 11 and 17 hours into the experiment the animal's aortic blood pressure slowly began to decline as a result of a loss of blood. At 20 hours into the experiment a transfusion was administered which increased the blood pressure and physiological parameters of the animal appeared to improve. At 19 hours into the experiment the animal's blood pressure was 130/90 mm Hg with a filling pressure of 0 mm Hg in the right atrium and 0 mm Hg in the left atrium. The pulmonary arterial pressure had a mean value of 25 mm Hg. Average power input of the electric motor was approximately five watts*. Bleeding from the chest stopped and it appeared that the second operation had succeeded in terminating thoracic bleeding.

Between 20 and 30 hours into the experiment the animal moved its head and had excellent reflexes. Average power measurements to the pump were between 3.9 and 4.2 watts. The animal was still maintained with respiratory assistance on 50% oxygen.

Between 40 and 50 hours into the experiment the animal was quiet but its reflexes were still good. At 47 hours into the experiment dopamine was administered to increase the arterial blood pressure which was decreasing. The blood pressure increased until the mean aortic pressure was between 130-150 mm Hg with a correspondingy increase in pumping power. Average power requirements were as high as 4.9 watts for a short period of time until the effects of the dopamine had dissipated. Dopamine was administered to test, in effect, the animal's ability to shift its blood pressures in response to a stimulant. Dopamine has the effect of constricting the blood vessels and potentially increasing the blood pressure and the cardiac output. Between 50 and 60 hours postoperative reflexes were still good. The animal was quiet, electric motor

*1.1 watts of the five watts was due to inherent mechanical losses in the electric motor bearings and brushes. Future power level references will not include these inherent losses.

temperature was within normal body temperature limits and all physiological parameters appeared to be normal.

Between 60 and 70 hours postoperative the animal's respiratory functions started to deteriorate. The respirator was adjusted to 100% oxygen and the tidal volume was increased to 2,400 cc. Still, power requirements at the blood pump were low with an average of about 3.9 to 4.1 watts of power delivered. Blood pressures ranged from an average of 100 mm Hg down to a low of 75 mm Hg. It became apparent that the animal's lungs were severely deteriorating irreversibly. Again, dopamine was administered to increase the animal's arterial blood pressure. Between 70 and 80 hours the animal's reflexes were still responsive. The animal was now very quiet and made no attempt to stand. The animal continued to require mechanical breathing assistance and 100% oxygen to maintain adequate blood gases. At 80 hours into the experiment the mean blood pressure was 135 mm Hg with an average power of 4.2 watts delivered from the electric motor. Between 80 and 90 hours postoperative respiratory assistance was unable to maintain adequate blood gases with the respirator, even though the animal was on 100% oxygen. Between 90 and 100 hours it became obvious that further post-operative care would not improve or even maintain the animal's condition. The animal's lungs appeared unable to provide sufficient respiratory assistance and at 100 hours the animal was terminated.

Autopsy Report:

The Holstein calf at termination weighed 105 kg. There was evidence of some subcutaneous edema of the legs and a very thick edematous plaque extending on the right side from the electric motor along the sternum. Using air driving pressure in the Monaghan of 40 cm of water, only about 1,100 cc tidal volume could be realized. At 100% oxygen the pCO_2 was about 60 and the pO_2 on 47. However, the pH was an acceptable 7.38. (This was blood from the pulmonary artery). Until termination the calf still had good reflexes and would respond to the slightest touch on the skin over the various parts of the body.

When the calf's chest was opened at autopsy, an excellent fit of the ERDA Blood Pump in the calf's chest was observed. The modified right ventricle seemed to eliminate any kinking in the pulmonary artery graft (as had been seen in earlier experiments). In earlier experiments the kinking of the pulmonary artery graft could easily have resulted in increased power requirements to circulate the blood through the restricted flow system.

At autopsy this calf had pneumonia with adhesions, particularly over the ventral portions of the right apical lobe. Furthermore, the lungs received a severe insult due to the foam that existed at surgery in the right ventricle and the pulmonary outflow tract.

There was 200 cc of pleural effusion in the right thorax and 1,700 cc of ascites fluid that was straw colored. The cardiac lobe of the right lung was kinked and totally collapsed the intermediate lobe of the right lung. The right lung was very heavy (1,700 gm) and very pneumonic. The left lung weighed 1,100 gm.

The left kidney weighed 240 gm, the right kidney weighed 260 gm. A massive pulmonary hemorrhage in the diaphragmatic lobe of the left lung contained an estimated 250 to 300 cc of blood. The left lung had purulent yellow bronchial secretions.

No compression of superior or inferior vena cava was noted, no compression of the atria was seen and, as has been mentioned before, there was an excellent fit of the heart into the chest cavity with the heart leaning close to the sternum of the animal. There was a small thrombus build-up initiating at the quick connect in the left atrium on the posterior wall, about 1½ cm from the atrial pressure tap. There was significant hemorrhaging around the electric motor. Peticheal hemorrhages of the serrosal surface of the cecum were observed. The urinary bladder contained 300 cc or normal appearing urine.

The liver weighed 3,150 gm. Some thrombus formation was evident in the diaphragm-housing junction of the blood pump near the drive shaft on the posterior aspect of the heart. It appears that the right diaphragm was touching the housing in the greatest curvature at full systole.

Summary:

1. The fit of the ERDA Blood Pump in the chest was improved with a modification of the right outflow port, i.e. the pulmonary arterial graft connection to the right ventricle. In earlier experiments this has always been kinked to a minor degree and probably has resulted in increased power demands for pumping adequate amounts of blood. In this experiment there was no kinking of the pulmonary artery graft which resulted in lower power demands.

2. Throughout the course of the experiment peak average power requirements from the electric motor never exceeded 5.1 watts overall. Average power for the experiment was only about 3.7 to 4.1 watts of power.

3. The electric motor operated well, the cooling system maintained the motor temperature at the normal body temperature of the calf. The flexible drive shaft operated well throughout the course of the experiment and at autopsy showed no serious signs of deterioration or kinking.

4. The ERDA Blood Pump itself and ventricles operated very effectively and pumped sufficient blood to maintain adequate blood gases and total body perfusion.

5. The use of the new plastic, polycarbonate quick connects increased the speed with which these connections of these grafts and great vessels were made and appear to work much better than the stainless steel quick connects used in earlier experiments. Although a preoperative pulmonary function analysis of the animal's lungs appeared to be normal, the animal actually did have severe bronchial pneumonia which, with the addition of the two surgeries, eroded the lungs to a point that postoperative care could not keep up with the lung's decreasing ability to maintain adequate oxygenation.

Summary of Total Artificial Heart Experiment No. 16 (TH75C6ERDA15A1, February 11, 1975):

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

Surgical Procedure:

A sternal split surgical procedure was performed on a female Hereford approximately 112 kg in weight. ERDA Blood Pump No. 2 was used with Avcothane-51 Elastomer ventricles and a smooth intimal surface. The blood pump ventricles were fitted with Bjork-Shiley pyrolytic carbon valves. The ERDA 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 preoperative lung function measurements made which indicated normal lung function for that size of animal. Surgery required 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 ventricular filling pressure of 4 mm Hg and a right ventricular 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 thoracic drainage tubes. At three hours into the experiment approximately 2600 cc of chest drainage had accumulated. At four 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 seven hours into the experiment the animal was attempting to stand. At 20 hours postoperatively the motor speed was still at 900 r.p.m. with an arterial pressure of 130/100 mm Hg. Left ventricular 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 markedly from 0 to 35 mm Hg, depending upon the animal's position. At 23 hours into the experiment it was decided to return the animal to the surgery table and reopen the chest in an attempt to correct the position sensitive condition that the blood pump had assumed during the experiment. At 24 hours the chest was again closed and the animal placed back into the postoperative cart. During this second operation the blood pump was loosened from its tethers on the sternum, 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 desireable.

At 25 hours into the experiment (two hours after the second surgery had occurred) 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 at 100/35 mm Hg for 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 maintain or improve the animal's condition. After the second operation had occurred 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 maintain a low left atrial pressure. The specific etiology of this consequence was difficult to identify. Several factors indicated that there was impingement of the inflow-outflow tract in the ventricle on the left side. This was possibly caused by pressure that the left chest wall was exerting upon the inflow-outflow tract of the left ventricle. This conclusion was based upon the following observations: (1) There was no evidence by the increased torque or decreased motor speed to confirm that high left lateral thoracic wall pressure existed on the pusher motor cup itself. The collapsible housing of 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. (2) A radiograph taken of the experimental calf when it was placed on its back in preparation for reopening clearly demonstrated that the long axis of the pumping ventricles and Scotch Yoke mechanism were not perpendicular to the long axis of the calf. (3) After reopening the chest and shifting the motor assembly further to the right and re-anchoring it, the left atrial pressures remained normal. (4) The flexible drive shaft was not placed through the diaphragm directly on midline to allow proper alignment 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 near the shoulder of the anterior margin of the electric implanted motor occurred within 48 hours. At autopsy it was determined that the motor was implanted immediately subcutaneously and not deep within the abdominal musculature. Previous experiences would indicate that the 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 ha reached normal values and rose to a high level of 41°C to 42°C. There were some rectal measurements taken with a mercury thermometer which registered over 107.6°F. At this temperature, within a very short period of time, many of the cytoplasmic proteins became irreversibly coagulated and denatured. At the time of reopening the chest, approximately 48 hours after implantation, the calf's temperature was so high that tissue was very uncomfortable to the gloved hand. The etiology of this persistent hyperthermia is unknown. There is no indication that this hyperthermia was from bacterial infection because: (1) The onset was too soon after surgery, (2) 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 and (3) 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 parboiled, as had been seen in a previous experiment without water cooling of the electric motor.

A very likely cause might have been pyrogens. This was the first use of Avcothane for fabricating ventricles for an ERDA Artificial Heart. These ventricles are first constructed with technical grade Avcothane-51 Elastomer and the final coating for the blood surface is medical grade Avcothane. Thus, the external surface of the ventricle, which has a large surface area, 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 adequately cleaned before being implanted in the animal. Furthermore, the question exists, is one layer of medical grade Avcothane coating the technical grade Avcothane sufficient to preclude the release of pyrogens from the technical grade material? Samples were submitted for pyrogen evaluation and cell culture toxicity evaluation of the technical and medical grade Avcothane. The result was, the liver appeared parboiled, which was due to the persistent high temperature of the animal.

Summary of Total Artificial Heart Experiment No. 17 (TH75C12A3ERDA17, April 8, 1975):

Experiment No. 17 was planned as a long-term evaluation experiment of the ERDA Bench Model 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-51 Elastomer with the modified soft shell dome.

Surgical Procedure:

A sternal split surgical implantation procedure was performed on a male Holstein calf of approximately 106 kg in weight. ERDA Blood Pump No. 2 was used with Avcothane-51 Elastomer soft shell ventricles with a smooth intimal surface. Bjork-Shiley pyrolytic valves were fit into the blood pump ventricles. 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 electric motor speed, torque, 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. Surgery lasted for approximately 3¼ hours with the animal on the heart-lung bypass for approximately 83 minutes.

Postoperative Recovery:

At three hours into the experiment the motor speed was 900 revolutions per minute. The average motor torque was approximately 9 oz.-inches. The motor temperature was 38.5° C. At this time the aortic pressure was 170/140 mm Hg with a 0.0 mm Hg right atrial pressure and 7 mm Hg on the left atrial pressure. The mean pulmonary pressure was 18 mm Hg. At six 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 total volume of 100 cc. At six hours and 20 minutes into the experiment the animal stood up and remained standing for approximately one hour. The animal at this time was maintained with a T-tube at 6 liters/min. with 40% oxygen. The animal appeared to be in excellent condition. Chest drainage had subsided and there appeared to be no bleeding problems from the thorax.

At 24 hours postoperatively the animal had stood up eight separate 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 reduce somewhat the pulmonary arterial pressure which had risen to a mean pressure of 43 mm Hg. During the 25th hour 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.-inches.

At 27 hours into the experiment the chest drainage tubes were removed since very little internal thoracic bleeding existed. The animal was extubated at 22 hours into the experiment. At 40 hours 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 being maintained at 1,025 r.p.m. for an average torque of approximately 10 oz.-inches.

Throughout the course of the experiment the electric motor temperature regulation system maintained the motor temperature at 38.5° C ± 0.3° C. From time to time, throughout the course of the experiment, the ventricular filling pressures, especially the left atrial filling pressure, would vary markedly, 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 terminated 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 water but was unable to eat throughout the course of the experiment. For this reason four to five liter mash-slurry mixtures were administered periodically for nutrition. At eight hour intervals streptomycin and penicillin was administered for infection. There were two episodes during the course of the experiment when the calf's temperature rose above 39.5 C. In the first temperature spike period the temperature returned to normal within one hour. The second temperature spike occurred near the termination of the animal, at approximately 260 hours. At termination the animal's anal temperature was 40.4 C.

During the 11 day survival of the calf the mean aortic pressure varied from 110 mm Hg to 150 mm Hg. The pulse rate for the animal varied from 120 b.p.m. to 145 b.p.m.

Summary:

This was our most successful experiment to date. One of the reasons for this success is due to the redesigning of the soft shell dome portions of the ERDA Blood Pump ventricles. These ventricles are made of two separate layers of Avcothane with two layers of mesh in between, separated by an air pocket. This procedure allows the ventricles to be much more compliant and the mesh minimizes the amount of expansion during systole.

The 11 day survival allowed evaluation of the blood pump under a variety of conditions. Also, no difficulty was found in maintaining the electric motor at normal body temperature with an external coolant system. There were no mechanical problems throughout the 11 day survival. The high left atrial pressure episodes could be due to a compression of the soft shell dome by the animal's rib cage. 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. The fluid (probably pericardial fluid) smelled of Spherophorous Nechrophilous. With four ribs removed (numbers 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 appeared normal and healthy, except for the atelectesis and edema in the anterior ventral margins. The left pericardial sac showed signs of fibrinous pericarditis with a necrotic odor mentioned previously. The ventricular housings were stained yellow, icteric, probably from bilirubin content. The pulmonayr 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 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. The animal had 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 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.

Summary on Total Artificial Heart Experiment No. 19 (TH75C16A4ERDA19, June 18, 1975):

Experiment No. 19 was planned as a long-term sterile experiment.

Surgical Procedure:

A sternal split surgical procedure was performed on a male Holstein calf of approximately 108 kg preoperative weight.

ERDA Blood Pump No. 2 was used with Avcothane ventricles having a smooth, intimal surface. The blood pump was fitted with Bjork-Shiley pyrolytic carbon valves. Due to the sensitive physical properties of Avcothane the blood pump ventricles cannot be autoclaved so the blood pump, drive shaft and electric motors were gas sterilized with ethylene oxide three days prior to surgery. This allowed 24 hours for gasing with ethylene oxide with approximately 48 hours airing time to remove residual ethylene oxide. Prior to surgery the animal was examined for pulmonary functions and found to have normal lung function. The animal was fasted for 24 hours prior to surgery. Preparation of the animal included anesthetizing with Brevane followed by Fluothane. Parameters monitored during the course of the experiment were aortic pressure, central venous pressure, left atrial 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.

Heart-lung bypass was approximately one hour 42 minutes with the total surgery lasting three hours 15 minutes.

Postoperative Results:

At approximately four hours into the surgery the animal's temperature returned to normal. Aortic pressures, pulmonary arterial pressures and inflow pressures were stable. Aortic pressure was 140/90 mm Hg, mean pulmonary pressure was 27 mm Hg, right and left inflow pressures were both approximately 8 to 10 mm Hg. For the next 24 hours the animal was maintained on the respirator, gradually reducing the oxygen concentration from 100% to 30% oxygen. Within 24 hours normal blood gases were achieved. However, the animal was not able to be extubated. At 30 hours the animal was stable enough to begin cardiac output evaluations. Cardiac output measurements were performed by using a dye dilution technique with the animal lying down and intubated, breathing on the respirator at 12 breaths per minute with a tidal volume of 1,000 cc. Dye dilution measurements indicated a cardiac output of approximately 9.5 L/min, with an electric motor speed of approximately 900 revolutions/min. Three measurements were performed with the dye dilution, two other cardiac output measurements indicated a cardiac output of 10.2 and 10.1 L/min. At 48 hours into the experiment the lung functions of the animal had not improved and it was apparent that further postoperative care would not enable the animal to be weaned off the respirator. At 50 hours into the experiment the animal was terminated.

Autopsy Report

Upon examining the artificial heart inside the chest cavity the relative position of the inflow atria cuffs and the atria appeared satisfactory, with no compression on the atria. Outflow, pulmonary and aortic grafts appear to be well positioned with no kinking in either graft. All four quick connects appeared to be sealing well. There was very little free and unclotted blood in the chest cavity. On examining the lungs the right lung weighed approximately 1,300 gm and the left lung approximately 1,100 gm.

There was marked evidence of consolidation and atelectesis in both lungs. The animal's liver was approximately 2,800 gm and appeared edematous and swollen. Upon examination of the kidneys they did appear to be enlarged, there were a few infarcts in the right kidney and numerous smaller infarcts in the left kidney. The animal's brain was not examined, as throughout the course of the experiment there was no evidence of neurological damage.

Summary:

This experiment allowed for the measurement of cardiac output capacities of the ERDA Mechanical Blood Pump. The length of the experiment was shortened because of pulmonary failure, which could have been due to air embolus and/or excess fluid consolidating in the lungs. The mechanical blood pump and drive train, along with the electric motor, all operated fine. There appeared to be no leaking of blood into the blood pump and due to the short-term nature of the experiment there was only very small deposits seen in the roll sock to each of the ventricles. Throughout the course of the experiment the animal was adequately perfused with the mechanical blood pump and maintained normal blood pressures. With the animal on the respirator, normal blood gases were realized. As the lungs became worse, higher respiratory pressures were needed on the support equipment. This condition persisted until such time that it was decided to terminate the animal at approximately 50 hours. Throughout the course of the experiment the power requirements for the electric motor never increased beyond an average of 5½ watts. The vacuum maintained on the blood pump was checked every hour and never varied from five inches of mercury. Cooling of the electric motor was maintained with a thermistor located on the electric motor, which would trigger a cooling pump to come on and off, maintaining the electric motor temperatures at 39.7 °C. This worked very well throughout the course of the experiment.

Summary of Total Artificial Heart Experiment No. 21 (TH73C21ERDA21, July 29, 1975):

The purpose of Experiment No. 21 was a long-term total heart replacement experiment to evaluate the ERDA Blood Pump driven by a water cooled electric motor implanted in the abdomen using a 3/16 inch drive shaft core and reinforced drive shaft casing. A stainless steel circumference band was fastened to the blood pump to eliminate any external compression of the soft shell flexible dome of the ERDA ventricle.

Surgical Procedure:

A sternal split surgical procedure was performed on a Holstein calf of approximately 110 kg in weight. The ERDA Blood Pump was WANL Pump No. 2 with Avcothane #3 ventricles. Bjork-Shiley valves were fastened to polycarbonate quick connects which promote rapid anasthemosis to be made to the great vessels during surgical implant of the artificial heart. The animal was anesthetized with Brevane followed by Fluothane throughout the course of the surgical procedure. Parameters monitored during the experiment are aortic pressure, pulmonary arterial pressure, left and right atrial pressure, electric motor speed and torque were monitored in addition to the vacuum maintained on the ERDA Blood Pump.

Preoperative lung function tests on the animal indicated normal performance. The heart-lung bypass time was approximately two hours with surgery requiring three hours and 45 minutes.

Postoperative Recovery:

Five hours into the experiment the animal's temperature had returned to normal. The animal was maintained on the Bird respirator at 10 breaths per minute with 40% oxygen. Blood gases were good. Motor speed was 900 r.p.m. and the average torque was approximately 10 oz. inches. Aortic pressure was 130/100 mm Hg with a right atrial pressure of approximately 28 mm Hg. The animal appeared alert and attempted to stand, but was still extremely weak and was unable to stand unassisted. At eight hours into the experiment the animal continued making attempts to stand. The calf was extubated and chest tubes were removed. At 25 hours into the experiment blood gases were normal, but indicated the need for additional oxygen which was supplied through a nasal tube.

At 26 hours the nasal oxygen was insufficient and the animal was reintubated. However, the animal did appear to be alert and was still attempting to stand. At 40 hours into the experiment the animal was still alert and attempting to stand. The animal was again extubated and fitted with face mask. At 44 hours the animal was reintubated because of increasing pulmonary insufficiency. At 80 hours into the experiment the animal had been intubated and extubated several times but was unable to breath unassisted without some nasal oxygen and/or mechanical assistance. However, the animal's reflexes were excellent and the aortic blood pressure was maintained adequately. However, the right atrial pressure became very negative, approximately -10 mm Hg. During the next 40 hours the animal's condition deteriorated and it became increasingly more difficult to maintain adequate blood gases via the respirator. At 120 hours the animal was terminated because further postoperative care would not improve or maintain the animal's overall condition.

Autopsy Report:

At autopsy the sternal split incision appeared to be closed, with no apparent signs of infection through the suture line. There was excellent fit of the blood pump in the thorax, with no kinking of the aorta and/or pulmonary arterial graft. No signs of compression, either of the left or right atrial cuff were evident. Upon examination of the artificial heart small adherent blood clots were found along the atrial cuff suture line and a large clot at the junction of the quick connect and valve seal. Numerous small clots were also found around the daiphragm-housing junction. The left ventricle was relatively free of clots near the aorta outflow. However, there were small clots on the orifice of the left atrial opening and numerous small clots along the left atrial suture cuffs. The thorax cavity was essentially clean, with little or no clotted blood surrounding the artificial heart. There was a large embolus in one of the major arteries of the left lung. Upon removal of the right ventricle a large clot was formed around the roll sock near the diaphragm-housing junction region.

In examining the lungs, the right lung was edematous and had a great amount of atelectesis. The left lung was totally atelectic with severe bolus emphysema. A small portion of the left lung was found between the blood pump ventricle dome and the band enclosing the ventricle. Damage to the lung was evident. There was no ascites fluid seen in the abdomen. The liver appeared in excellent condition with no large infarcts. A few infarcted areas existed in the right kidney. The left kidney had a good appearance.

Summary:

The experiment provided a practical evaluation of the use of a protective band or strap around the ventricle dome to prevent external compression of the soft flexible artificial heart dome. However, it was evident at autopsy that a portion of the lung was trapped between the protective band and the dome, causing damage to the lung tissues and perhaps compromising the filling of the left ventricle. The five day evaluation of the Avcothane surface indicated that significant thrombus buildup can accumulate in the roll sock region. This thrombus deposit can grow and extend to the outflow ports, thus compromising the action of the Bjork-Shiley tilting disc valve. Power requirements throughout the course of the five day experiment indicated that between four and six watts of power were sufficient to adequately perfuse the animal. The mechanical blood pump operated well throughout the course of the experiment as well as the electric motor and the coupling flexible drive shaft. The use of the Avcothane #3 ventricles for a long period of time would require apparently the administration of an anticoagulant therapy.

Tentative cause of death was attributed to pulmonary insufficiency. Broncho-pneumonia appeared on the histopathology slides and was attributed to the extended period of time the animal was maintained on a respirator.

Summary of Total Artificial Heart Experiment No. 22 (TH75C23ERDA22, August 13, 1975):

The purpose of Experiment No. 22 was a long term total heart replacement experiment with the ERDA Blood Pump designed to evaluate the implanted pump which is driven by a water cooled electric motor implanted in the abdomen. The blood pump was driven via a flexible 3/16 inch drive shaft coupled to the electric motor. The shaft was contained in a reinforced casing. Also, evaluation was planned for radio frequency glow discharge (RFGD) and dye treated ventricular surfaces.

Surgical Procedure:

A mid-sternal split incision was performed on a 012 kg Holstein calf. WANL Blood Pump No. 2 was used with a flexible drive shaft No. W-36. Silastic ventricles with fibrilized surface were attached to the blood pump. Pretreatment of the Silastic ventricles consisted of radio-frequency glow discharging of the ventricles and cuffs. After five minutes of RFGD treatment at 200 μ Hg pressure in argon, the ventricles and cuff were treated with 0.1% by weight amaranth dye. The ventricles were allowed to absorb the dye overnight for approximately 14 hours. Following this the ventricles

were rinsed once with saline and the complete blood pump and ventricle assembly was autoclaved prior to surgery. The rationale for using this pre-treatment process stems from recent success in using this series of treatments on Spark's Mandrils implants to promote tissue in growth and minimize platelet deposition and to promote an overall improvement in the non-thrombogenicity of the blood contacting surfaces.

Preoperative lung functions were performed on this animal and indicated that the animal had normal functional residual capacity as well as adequate tidal volume.

Preoperative anesthesia was initiated with Brevane induction followed up with Fluothane. Pressures monitored during surgery and postoperatively included aortic and pulmonary arterial pressures, left and right atrial pressures, motor speed and torque were monitored as well as the vacuum maintained on the bench model blood pump. Bypass time was approximately one hour 42 minutes with the total surgery lasting a little over three hours.

Postoperative Procedure:

There was very little hemorrhage from the thoracic cavity or from the abdominal pocket containing the electric motor. After approximately eight hours there was only 650 ml of blood in the chest evacuation bottles. Then a severe hemorrhagic episode occurred releasing approximately 1800 cc of highly oxygenated blood through the chest drains. Two (2-liter) bottles of blood were immediately set up for transfusion and blood was rapidly transfused into the animal. Consideration was given to reopening the chest to localize and correct the hemorrhage. Suddenly the hemorrhaging ceased and when no further bleeding was evident the chest drains were pulled. There was very little hemorrhage issuing from the abdominal pocket. The pressure lines had a Velour covering and were exteriorized through the wall of the right chest. The Velour was not properly placed and only one of the Veloured lines perforated the skin. During surgery the lungs were maintained in a high volume condition and were intermittantly inflated and deflated back to that level.

The animal was extubated early in the course of the postoperative experiment with no subsequent disfunction of the lungs or need for oxygen support. After the chest drains were pulled the calf received Persantin, Coumadin and aspirin as per the modified Mansfield protocol. The calf was assisted in standing on the first postoperative day and was able to stand unassisted on the second and subsequent days. The animal was active throughout the experiment and was exercised by walking on the treadmill several times. The calf's body weight gain was good after allowing a recovery period from the surgical intervention. However, towards the end of the experiment weight gain ceased and appetite appeared somewhat reduced.

On Friday, August 22 an electrical power failure occurred and the emergency power system failed to function because of intermittant power disruptions. Thus, for about 20 minutes cardiac output in the animal was intermittant and the calf was re-intubated and placed on oxygen. The calf suffered severe trauma during this interim. The calf responded well, however, and the following day was standing and eating.

Blood transfusions were administered on the 10th and 16th days (2 liters each) and on the 20th day packed red blood cells in the equivalent of two liters were administered. On Thursday, the 28th day of August, "Critter" (the name given to the calf) appeared in excellent condition. On Tuesday, September 2, it was obvious the calf's condition began deteriorating. The calf's hair was disheveled and he ceased gaining weight. His appetite abated and he went off his feed. On Tuesday afternoon, September 2, in his 21st day he was placed on the treadmill and walked about 30 seconds. The treadmill was set at a fast pace and the animal fell (or tripped) on the treadmill. Subsequently the calf stood up again and was returned to the stall. Later in the afternoon he ate a little solid food. However, early on September 3, late in his 21st day, body temperature started dropping at the rate of about 0.2 to 0.3° C per hour. The hematocrit, over an 8 to 9 hour period, dropped from 21 to a low of 13. The animal was lethargic and listless. Atrial pressures had continued to remain high over the last week of the experiment. The mean pulmonary artery pressure was between 40-50 mm Hg, the aortic pressure also remained high. The liver was palpable on the 20th day of the experiment. The animal exhibited nystagmus bilaterally. However, blood gases could be maintained with 400 cc of whole blood and packed red blood cells. The packed cells from approximately 2 liters of blood were administered and the hematocrit was increased to 20%. The calf continued to deteriorate and no definitive diagnosis could be made for deterioration. It was assumed that the administration of packed cells resulted in serum and coagulation products which generated thrombus within the artificial heart and drove emboli into the brain. The bilateral nystagmus persisted becoming worse with time. There was a very slight trace of blood in the mucus secretion of the nasal passages. Breathing was rapid increasing CO_2 removal and thus raising the pH. Attempts to compensate for this were made by giving nasal oxygen at about 3L/min. rate. This increased the pO_2 and decreased pCO_2, thus lowering the pH.

On the 21st day of the experiment the animal extended his behind legs, driving himself forward in the cage with severe rigidity, which is indicative of cerebral emboli. Early in the afternoon Critter went blind, unresponsive to sight and sound. His right pupil was markedly dilated and his left was moderately constricted. The diagnosis was made of thromboembolism into the brain. He continued to deteriorate and his temperature decreased despite the fact that electrical blankets were placed over him. At one point in time during this period all of his blood pressures went very high, the aortic pressure in excess of 200 mm Hg, the pulmonic pressure in excess of 200 mm Hg. The electrical was heavily overloaded. Suddenly about 1 liter of blood pulmonic in origin gushed from the nose and mouth. Then Critter, Experiment No. 22, died. Physiological data obtained from Critter during the course of the experiment is given in Figure XI-11.

Autopsy Report:

There was no evidence of the right heart failure syndrome. There was total absence of any ventral edema of the brisket area around the thoracic inlet. The pouch containing the electric motor was very clean with no evidence of infection. There was an absence of aroma, no visible pus, and the pouch was enchased in very healthy, viable appearing tissues. The umbilical cord was infected around the skin exit and this infection persisted approximately 1½-2 inches along the umbilical cord. This was

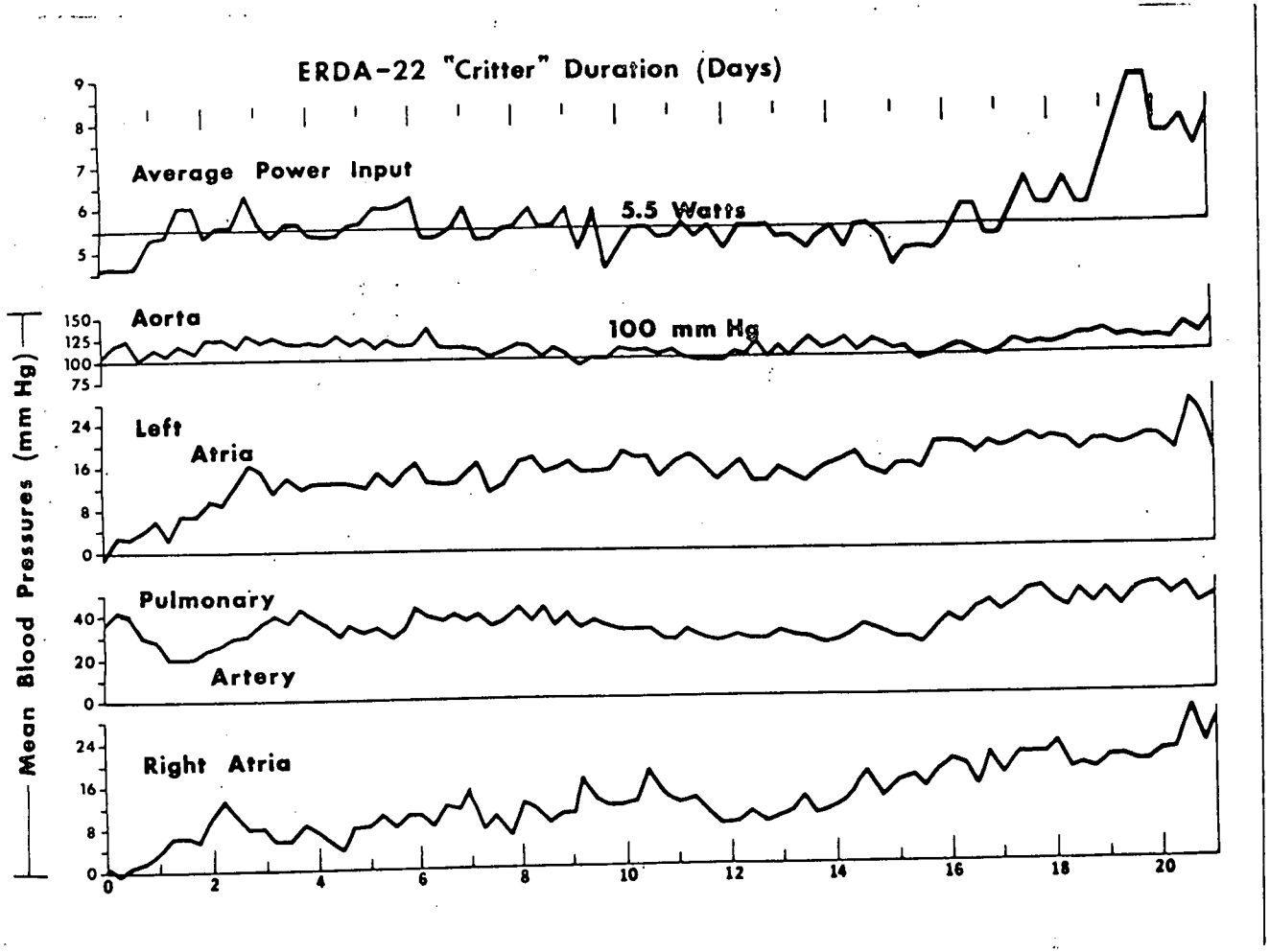


Figure XI-11 Physiological Data Obtained from Experiment ERDA 22.

probably the source of the spiking body temperature. As the animal moved this cord would tend to slide in and out transporting infection and debris into the marsupialized area. The drive shaft had a great bow curvature in it. Probably this exaggeration of curvature was due to the suspended position of the animal during autopsy.

The lungs were very heavy and hemorrhagic. On the sub-pleural as well as the cut surface they appeared to have multiple small hemorrhages, and multiple thrombo-emboli were found scattered throughout the parenchyma. There were no large thrombo-emboli in the pulmonary arteries. The position of the heart within the chest was very good. The blood pump was not tethered to the sternum and this blood pump was implanted without the protective band over the compressible ventricle domes. The mediastinum and the left pericardial wall were still intact. There were some blood clots over the top of the left pumping diaphragm around the left atrial suture line. The pericardial sac was not unduely thickened, however. There was no evidence of pressure necrosis. All of the anastomotic sites were very clean and very smooth. The inside of both Dacron vascular grafts were both well embedded with fibrous connective tissue. The atrial cuffs were very clean and the valves were very clean. Upon opening the ventricles there was a thin layer of proteinaceous material over the fibrilized surface, but very easy to remove and there was speculation that, in part at least, this occurred post mortem.

There was a small amount of attached thrombus in the roll sock area. The diaphragm-housing junction in the silicone ventricles is much reduced over the poly-urethane ventricles and was very clean. There was no evidence of blood under the dispersive coating over the stainless steel blood pump jacket. There appeared to be a denuded area over the diaphragm-housing on the right side that may have rubbed upon a rib but it appeared that the diaphragm did not touch the housing during systole. The appearance of the blood pump externally and internally was very good for a 21 day experiment.

The kidneys had two infarctions, one in each kidney, relatively large and somewhat old. There appeared to be gross intraglomerular hemorrhages throughout the parenchyma, primarily situated, however, at the cortex and subcapular area. The kidneys were in very good condition. Kidneys with a Dacron fibrilized silicone rubber ventricle surface type were in the best condition yet observed after 21 days in an ERDA experiment.

The spleen was unremarkable. There were about 250-300 cc of ascites fluid, not too unusual. A remarkable characteristic was the severe diffuse petechial hemorrhages in the subcerosul and subnecrosal surfaces of all organs examined: viz: the periotoneum, the mesenteries, the intestinal walls and the urinary bladder. There were ulcers in the abomasum and also petechial hemorrhages. There were petechial hemorrhages of the subnecrosa of the reticulum and over the surfaces of the rumen. The urinary bladder contained approximately 750 cc of very dark urine and there was edema in the distal segment of the anterior mesentery, particularly along the attached border of the abomasum. This may have been a result of abomasul ulceration.

The spleen was unremarkable, contracted, small, with some subcapsular hemorrhages of the free margin and tip. Within the interior vena cava at the margin

of the posterior edges of the liver there was one small subendothelial hemorrhage and there were some fatty appearing deposits on the endothelial surface. There was blood in the interior chamber of the right eye that had coagulated and there was severe subarachnoid hemorrhages over the entire brain, almost 3 to 4 mm in thickness, to the left of the origin of the optic chiasma, covering the entire ventral surface of the cerebral hemisphere. This explained the blindness and nystagmus pupillary dilation of the right eye. Subarachnoid hemorrhage was severe and profuse, extending down the spinal cord.

Conclusion:

The appearance of the animal of the autopsy indicated a severe thromboemboli phenomenon of multiple small emboli dispersed throughout the arterial and pulmonic vasculate. There were no subcapsular or intraparenchymal hemorrhages within the liver; thus, further substantiating the arterial and pulmonic circulatory thromboembolism, since the liver gets its primary blood supply from the portal system. The hemorrhages accompanying the occlusion of the small blood vessels accounts for the tremendous blood loss within the parenchyma and tissues throughout the body.

The cerebral disintegration of the animal was explained by the subarachnoid hemorrhages. The triggering mechanism and/or origin of these multiple thromboemboli is not fully known. Possibilities include (a) a localized phenomenon on the Dacron fibrilized surfaces of the heart and the raw Dacron vascular grafts, triggering the thromboembolic mechanisms (b) A true disseminated intravascular coagulopathy (DIC), the triggering mechanism unknown and a question as to "can this truly occur in a animal under Persantin, Coumadin and aspirin, and hyperanticoagulated, the way this animal was?" A cursory evaluation of the hematological values indicated that this coagulopathy initiated at the time of power failure at about 212 hours. Indeed, some of the coagulative factors did change at this point, never to recover again, i.e. platelet number, etc. However, the fulminating condition of the animal at the terminal stages may preclude that supposition.

Another as yet unexplainable situation might be the role of sodium iodide in the anticoagulated animal.

In summary, it would appear that Dacron fibrilized silicone hearts on the ERDA pump with anticoagulation should be continued and the role of the glow discharge and dye treatment of the vascular graft, in combination with anticoagulative therapy, should be elucidated.

Summary of Total Artificial Heart Experiment No. 24 (TH75C33S11ERDA24IVBM2, November 14, 1975):

Experiment No. 24 was a long-term sterile experiment designed to evaluate the IVBM oil-filled blood pump powered by a water cooled electric motor implanted into the abdomen of a calf.

Surgical Procedure:

A mid-sternal implantation procedure was performed on an Angus (Whiddison) calf of approximately 111 kg weight. The blood pump was WANL Pump No. 4, IVBM model, fitted with Silastic ventricles covered with a layer of Dacron fibrils on the blood contacting surfaces. The driving system was an internally implanted electric motor, water-cooled, with an oil seal separating the electric motor from the sperm oil in the drive shaft coupling system. The animal was anesthetized with Brevane followed by Fluothane. The total bypass time was approximately one hour 56 minutes. The total surgery lasted 3½ hours. During surgery, while priming the blood pump, air was entrained in the right side of the heart. The chest was flooded with saline prior to initiating the pumping in an attempt to correct the condition. After the quick-connects were seated the chest was closed, chest tubes were inserted and the excess saline solution was removed.

Postoperative Recovery:

Due to the air pumped into the right side of the heart during surgery there was an onset of pulmonary hypertension and acute airway obstruction. This led to ventilator dependency of the animal coming off of the table. The evening following surgery, at approximately 12 hours postoperatively, the animal tried to stand several times, but was dependent upon the ventilator. At approximately 43 hours the chest tubes were removed after the animal had lost approximately 9,400 cc of blood. However, this fluid was continuously replaced throughout the course of the experiment. The animal had several convulsions during the first 24 hours postoperatively. It was decided to attempt to support the pulmonary functions with the ventilator. The calf was placed on intermittent mechanical vantilation after doing well off of PEEP (on the 74th hour). Pressure tracings suggested a drop in atrial pressure at the 81st hour and subsequent acidosis. Although the left atrial pressure became elevated, this eventually declined to approximately 2 mm Hg. Reflexes then disappeared and the animal was terminated at 83 hours.

Autopsy Results:

Upon examination of the thorax there was approximately 650 ml of clotted and unclotted blood in the right and left chest combined. There was no kinking or compression of the atria or great vessel connections. However, it was noted that the right atrial quick connect was incompletely closed and could have possibly accounted for the loss of blood throughout the course of the experiment. Examining the inside of the ventricles we found that puckers, or pleats, in the diaphragm (where it rolls over the edge of the pusher cup) had small thrombus deposits. This has been seen in other experiments. The left ventricle and atrium were cleaner and much more free of deposit than the right atrial cuffs and ventricle. The left ventricle had been treated prior to surgery by radio-frequency glow discharge in Argon for approximately five minutes.

The lungs appeared to have consolidation of the apex of both lungs and dependent portions were also consolidated. There was hepatization of both lungs with severe hepatization in the right. There was no ascites seen but the liver was engorged and its appearance, on section, was normal. There was an absence of infarcts in the right kidney. However, the left kidney had areas of blushing but no emboli were seen. Again, tissue samples were sent to histology for analysis of any tissue that might contain sperm oil. Histopathology reports proved negative. Tentative cause of death was pulmonary failure and hemorrhaging into pleural cavity due to quick connect misplacement. The pulmonary failure most likely occurred when air was introduced into the vascular system through the right ventricle, during the surgical priming sequence.

Conclusions:

The mechanical system, including the blood pump, drive shaft and electric motor all functioned well. There was no indication of sperm oil leaking out of the IVBM blood pump chambers. The drive shaft worked well as far as the electric motor and the oil seal on the motor. Precautions taken for future experiments will be to eliminate any air from getting into the vascular system through the quick connects during the priming procedure and secondly ensuring that the quick connects are completely seated by using a small inspection mirror. Again, oil drained from the pump chamber appeared to be darkish brown in color. Samples were analyzed for the possibility of blood content, but tests proved negative with no traces of blood seen in the sperm oil. After the blood was removed from the animal's chest the outer housing on the ventricle was removed and upon inspection it was found that the oil had effectively retained the roll-sock configuration of the diaphragms.

Summary of Total Artificial Heart Experiment No. 27 (TH76C1S15ERDA27, January 20, 1976):

This experiment was planned as a long-term sterile experiment to evaluate the bench model blood pump powered by a water cooled electric motor implanted in the abdomen and for evaluation of the blood pump performance when the animal's own natural aortic and pulmonary artery valves are left intact.

Surgical Procedure:

A mid-sternal thoracotomy was performed on a red Angus calf, male, approximately 112 Kg in weight. The artificial heart was the bench model blood pump 3 with Silastic ventricles coated with a smooth silicone dispersion on the blood contacting surfaces. The right atrial cuff was treated prior to autoclaving with radio-frequency glow discharge using Argon as the working gas for approximately five minutes. When the animal was placed on the table and prepped prior to surgery there were clear chest sounds that were abnormal, and a reduction was noted in the functional residual capacity (FRC). Total bypass time was approximately two hours five minutes, and considering that both the natural aortic and pulmonary valves were prepared for use with the pump, bypass time was acceptable.

Postoperative Course:

At one hour into the experiment the animal's mean aortic pressure was 100 mm Hg (the right atrial pressure was 5, the left atrial pressure was a mean of 5 mm Hg), the mean right ventricular pressure was 15 mm Hg. At seven hours postoperatively the animal's reflexes were excellent. The pump was turned off for two seconds to determine regurgitation through the natural aortic valve. It was found to be holding excellently with a slow decay time in the aortic pressure. With the excellent function of the animal's natural aortic and pulmonary valves we were able to maintain adequate circulation while keeping the pump speed at approximately 600 r.p.m., or a beat rate of around 80 to 85 beats per minute. Consequently, torque measurements were lower than normal, as well as power requirements. The animal had to be maintained with respiratory assistance on a Bird respirator. At 18 hours into the experiment cardiac output determinations were made with a thermal dilution technique. Cardiac output measurements indicated flows of 2.5 and 2.7 liters per minute and pump speed of approximately 650 revolutions per minute, corresponding to approximately 80 beats per minute. A very low filling pressure of -4 mm Hg on the right side and -6 on the left side. At approximately 19 hours into the experiment the animal's reflexes diminished very rapidly. Pulmonary functions decreased very quickly as well. It was determined that further postoperative care could not help this animal so the experiment was terminated at 20 hours.

Autopsy Results:

Upon examining the thorax there was no free unclotted or clotted blood present. The fit of the artificial heart inside the chest was excellent with no kinking of the aorta and/or pulmonary graft. There was no compression of the atria cuff. When the artificial heart was removed both the pulmonary and the aortic valves were competent. However, upon examining the lungs there was severe congestion and all portions of the lungs sunk when immersed in water. The liver was enlarged, but appearance upon section was unremarkable. The kidneys had a capsule that stripped off easily. The cortex was dark purple and the medula was congested. No infarcts were seen on the left or right kidney. Tentative cause of death was pulmonary edema. The animal suffered edema during the initial phase of the pumping while still on the surgical table. Approximately 1 liter of fluid was drained from the animal's lungs, while the chest was being closed.

Conclusions:

Although this animal was terminated early into the experiment due to pulmonary edema, sufficient power measurements were made to assess the effectiveness of saving the natural pulmonary and aortic valves. Approximately 30 to 45% power savings were noted when compared to earlier experiments where both outflow valves were of the Bjork-Shiley type. In addition to an increase in the efficiency of the pump system the electric motor could be operated at reduced r.p.m. while maintaining adequate aortic pressures and vascular circulation. Under normal circumstances the blood pump would

run at approximately 900 r.p.m. which corresponds at 120 beats per minute. During this experiment the speed ranged from 600 r.p.m. to 900 r.p.m. Throughout the course of the experiment the electric motor, drive shaft and blood pump operated satisfactorily. The increase in cardio-pulmonary bypass time required to save the natural aortic and pulmonary valves was deemed acceptable. Because of the success of this technique it was tried on all future animal experiments with the DOE system.

Summary of Total Artificial Heart Experiment No. 29 (TH76C3S16ERDA29, February 5, 1976):

This was a long-term sterile experiment to evaluate the bench model blood pump powered by a water cooled electric motor implanted in the abdomen and to evaluate the blood pump performance and power requirements when the animal's natural aortic and pulmonary valves are left intact. Evaluation was also planned of using diaphragms not attached to the pusher cups.

Surgical Procedure:

Surgery was performed on a Hereford bull calf weighing 95 Kg at the time of implantation. The standard implantation procedure and mid-sternal split incision was performed with a pouch created for the electric motor in the abdomen. The lungs were normal and the surgical procedure was uneventful. Then, while attempting to connect the aortic quick connect to the outflow ring (the pulmonary artery valve and the aortic valve were salvaged in this case), a tear was made into the ventricular outflow tract. This necessitated disconnecting the connector and patching it with Dacron felt, both inside and outside. After careful assessment an aortic Bjork-Shiley outflow valve was implanted in the valve ring and the aortic leaflets were left intact. Efforts were made to keep the left atrial pressure low.

Part of the lengthened time for the implantation of the heart and bypass time was due to the occurrence of a large wrinkle and folding of the diaphragm over the pusher cups as vacuum was applied to the inside of the blood pump. This caused some delay during the implantation.

The problem with the ventricular outflow tract required return to the heart-lung machine and the total pump time was extended to 3 hours and 2 minutes. The final transition from the heart-lung machine to the artificial heart was uneventful.

Postoperative Recovery:

The pCO_2 was onsistently high at 50 to 54 mm Hg, but the pH remained normal. The pO_2 in the blood was held between 60 and 120 mm Hg. On the third postoperative day the calf ate some grain and hay. The calf continued to drink water from the first day postoperative. The fifth day 4 liters of warm water containing the flushings of a healthy beef rumen content was administered by a stomach tube. The blood pressures and the blood chemistries remained within normal ranges. There was some arterial hypertension evident, so the blood pump was frequently run at a slow rate. All evidence

indicated that both the natural aortic and natural pulmonary artery valves were functioning properly. The animal was placed on Persantine, Coumadin and aspirin at 48 hours. At about 125 hours the left atrial pressure rose sharply, peaking above 45 mm Hg-mean, which caused pulmonary edema characterized by a dramatic increase in PCO_2, decrease in pO_2 and a dramatic fall in the blood pH. The calf was in obvious respiratory distress with pulmonary edema evidenced by foaming and frothing at the mouth. Two doses of Lasix (40 mg each) were given at 15 minute intervals in an effort to reduce the blood volume and lower the left atrial pressure. The aortic pressure remained high and the peak diastolic pressure fell to near zero for a period of time, indicating an improper functioning of the left ventricle or valves. The calf was intubated and placed on PEEP to alleviate the pulmonary distress. The calf died approximately 1½ to 2 hours later. At this time a large amount of blood was pulled into the vacuum system -- probably via the blood pump, the electric motor and into the central vacuum system.

Autopsy:

At autopsy the following morning the lungs were markedly edematous with very moist excudate in the bronchial respiratory tree and only part of the dorsal lobes of either lung would float in water. There was no evidence of pulmonary embolization. There were some small infarcts in the kidneys.

The chest itself was relatively clean except for some recent hemorrhaging into the thorax along the site of the mediastinal incision. The natural aortic valve was patent and functioned under static water pressure. There was a small amount of edema and/or hemorrhage in the roots of the coronary cusps of the aortic valve. The short aortic graft and ventricular outflow tract appeared unremarkable. The pulmonary outflow tract, however, was quite hemorrhagic. There was a shiny, red thrombus lining in the pulmonary vascular graft and the infundibulum of the right ventricular outflow tract was very hemorrhagic throughout the wall, with a large amount of edema and hemorrhage in the roots or bases of the pulmonary valve cusps. Both valves were photographed and sections submitted for histopathological evaluation. Upon dismantling the blood pump extensive blood was found in the Scotch Yoke mechanism.

There was a rectangular worn spot along in the middle of the dependent part of the roll sock of the left diaphragm. The Silicone rubber had been worn off of the Dacron mesh supporting material and was exposed and eroding in three or four places. Where this Dacron mesh had been worn, the inner layer of Silicone rubber had been perforated, allowing blood to pass from the left ventricle into the pumping mechanism.

As the right side of the diaphragm was removed and housing on the right side exposed, massive blood clots were found in the blood pump. After removing the pusher cup it was observed small steel ball bearings had escaped from their race in the linear carrier bearing where the left pusher cup attaches to the shaft. Since the pusher cup had not been fastened to the diaphragm it worked loose simply by counter-clockwise rotation, thus allowing sufficient space for the ball bearings to escape their race.

The unusual worn spot on the diaphragm was in juxtaposition to the carrier bearing that rides on the insert race on the inside of the pump housing. It would appear that the roll sock got under that bearing repeatedly and eventually was damaged, allowing entrance of blood from the ventricular cavity into the pumping mechanism.

The mechanism was cleaned and returned to Westinghouse for their evaluation.

Conclusions:

There is a definite power savings realized by utilizing the animal's own natural outflow valves (aortic and pulmonary). The resulting increase in over-all pump efficiency is about 30 to 50%. The attempt to operate the pump with the roll sock diaphragms not attached to the pusher cups was unwise and caused delays during surgery and led to the demise of the animal.

Summary of Total Artificial Heart Experiment No. 30 (TH76C4S17ERDA30IVBM4, February 19, 1976):

The purpose of this experiment was to evaluate the IVBM pump powered by a water cooled electric motor, saving the animal's natural aortic and pulmonary valves. The intima of the ventricles was smooth Silastic with dispersion coated surface.

Surgical Procedure:

A 108 Kg male Holstein calf was employed, using the mid-sternal split. The artificial heart was WANL pump No. 4, IVBM model fitted with Silastic ventricles which were dispersion coated.

Bypass time using the Harvey oxygenator was 2 hours 48 minutes. Prior to starting CPB the animal fibrillated and circulation had to be maintained by cardiac massage.

The switch from cardio-pulmonary bypass to an electric motor was accomplished without any left atrial hypertension, even though it was necessary to go on and off bypass three times because of a malfunctioning electric motor. During the next 26½ hours constant monitoring of the heart rate and left atrial pressures was required in order to maintain proper circulation during this period of rapidly fluctuating motor speeds.

The animal remained intubated throughout this period in preparation for a second surgical procedure, at which the electric motor was replaced by a backup motor. At 26½ hours this second operation was performed under general anesthesia. The abdominal wall wound was opened and the electric motor exposed, shut off and disconnected while a second motor was connected and initiated to resume the circulation. The circulation was arrested for 20 seconds and the motor was up to speed in 45 seconds. A second circulatory arrest of 30 seconds was required to pass the umbilical cord through the skin hole.

After changing the electric motor the calf was briefly extubated but required reintubation. The calf slowly deteriorated and was terminated at 98½ hours. During the experiment, power levels varied from 9 to 13 oz. inches and the motor speed was erratic with heart rates at times exceeding 200 beats/min. Simultaneous atrial pressures showed that the left atrial pressure averaged 10 cm above right atrial, the right atrial pressure being negative early in the experiment and positive later in the experiment. The animal received anticoagulant, according to Mansfield's protocol.

Autopsy:

Autopsy revealed 5 small infarcts in each kidney. There was thickening of the pulmonary alveolar wall and slight pulmonary capillary congestion. The liver was normal. Thrombi was present on the Bjork-Shiley valve rings, especially where the struts meet the ring.

Conclusion:

There was oil found in the electric motor which effected the speed control feedback circuit. The heart valves functioned well in spite of evidence of hemorrhage into the base of the cusps.

Summary of Total Artificial Heart Experiment No. 32 (TH76C7S24x2ERDA32-IVBM4, March 23, 1976):

The primary objective of this experiment was to optimize inflow orientation of the Bjork-Shiley valves to decrease regurgitation and improve efficiency of the heart. Mock circulation experiments had shown that the greater cardiac output could be obtained with the inflow valves opening towards the outflow valves. Secondary benefits of lower right and left atrial pressures were also expected.

Surgical Procedure:

A 118 Kg Holstein calf was selected for implantation. The oil-filled and totally sealed IVBM pump, Model No. S24x2 (Silastic with dispersion-coated intima) was implanted into the chest and the motor placed within the abdominal wall during two hours 21 minutes of cardio-pulmonary bypass. The natural aortic and pulmonary artery valves were salvaged. Left and right atrial pressures, right ventricular pressures, aortic pressure of coronary artery and pulmonary artery flow were all monitored.

Postoperative Recovery:

Motor speed was increased from the normal 550 r.p.m. and torque of 7.5 oz. inches to 1100 r.p.m. and torque of 11 oz. inches, in an attempt to decrease the left atrial pressure. After 70 hours of pumping the left atrial pressure could not be maintained below 20 mm Hg and climbed to 29 mm Hg. However, the clinical condition of the animal was good and the calf repeatedly tried to stand. He was extubated after 16 hours postoperative.

Because of apparent imbalance between the right and left hearts it was decided to equalize after-loads to both ventricles by banding the right ventricular outflow tract. At 146 hours a second operation was performed to reduce the left atrial pressure to 15 mm Hg while maintaining the right atrial pressure at 5 mm Hg. The torque, however, reached 16 oz. inches at 1000 r.p.m., and 12 oz. inches at 600 r.p.m. This caused a transformer to fail 15 hours later. The experiment was terminated at 162 hours because of failure of the motor controller transformer.

Conclusions:

Hemodynamics: Flows as high as 13.6 L/min. were measured at 19 hours postoperatively, compared to 6.4 L/min. for the natural heart at surgery. Atrial pressure spikes were still prominent and at four hours postoperatively were measured as follows: Right atrial pressure fluctuated -30 to +15, or 45 mm Hg (mean -7.5 mm Hg). Left atrial pressure fluctuated -17 to +13, or 30 mm Hg (mean 0 mm Hg). It appeared that either the right heart outpumped the left heart or that bronchial flow was excessive.

Mechanical Problems: Hardware problems encountered were a coolant leak into the abdominal motor pocket and a loose electrical connection in the cable from the motor to the animal. The transformer failed due to overloading.

Power Consumption: Varied from 4 to 10 watts.

Autopsy: Showed thrombus generation around both inflow valves, which seemed to originate from around the valve ring polycarbonate junction. Both kidneys showed evidence of infarctions.

Summary of Total Artificial Heart Experiment No. 33 (TH76C11S21IIERDA33-IVBM8, July 13, 1976):

The primary objective of this experiment was to evaluate the IVBM blood pump with modified ERDA II style Silastic ventricles. The ventricles had been modified as follows: Right Ventricle: Regular outflow tract, 30 mil. thick dome, reduced displacement volume (i.e. right pusher cup reduced in volume by 9.4%) and Bjork-Shiley inflow valve in No. 2 positions. Left Ventricle: Epoxy covered (for added rigidity) outflow tract, 30 mil. dome, unmodified displacement volume and Bjork-Shiley inflow valve in No. 4 position. It was expected that with these modified ventricles (specified as ERDA II ventricles) a balanced output between the left and right ventricle would be achieved. The calf's own natural pulmonary artery and aortic valves were used as outflow valves for the pump. Electric motor No. 2 was implanted with shaft No. W-122 and a vacuum drawn through the shaft casing and blood pump.

Surgical Procedure:

A 97.5 Kg female Holstein calf was selected for the experiment. The modified ERDA blood pump was implanted into the thorax via a sternal split surgical procedure.

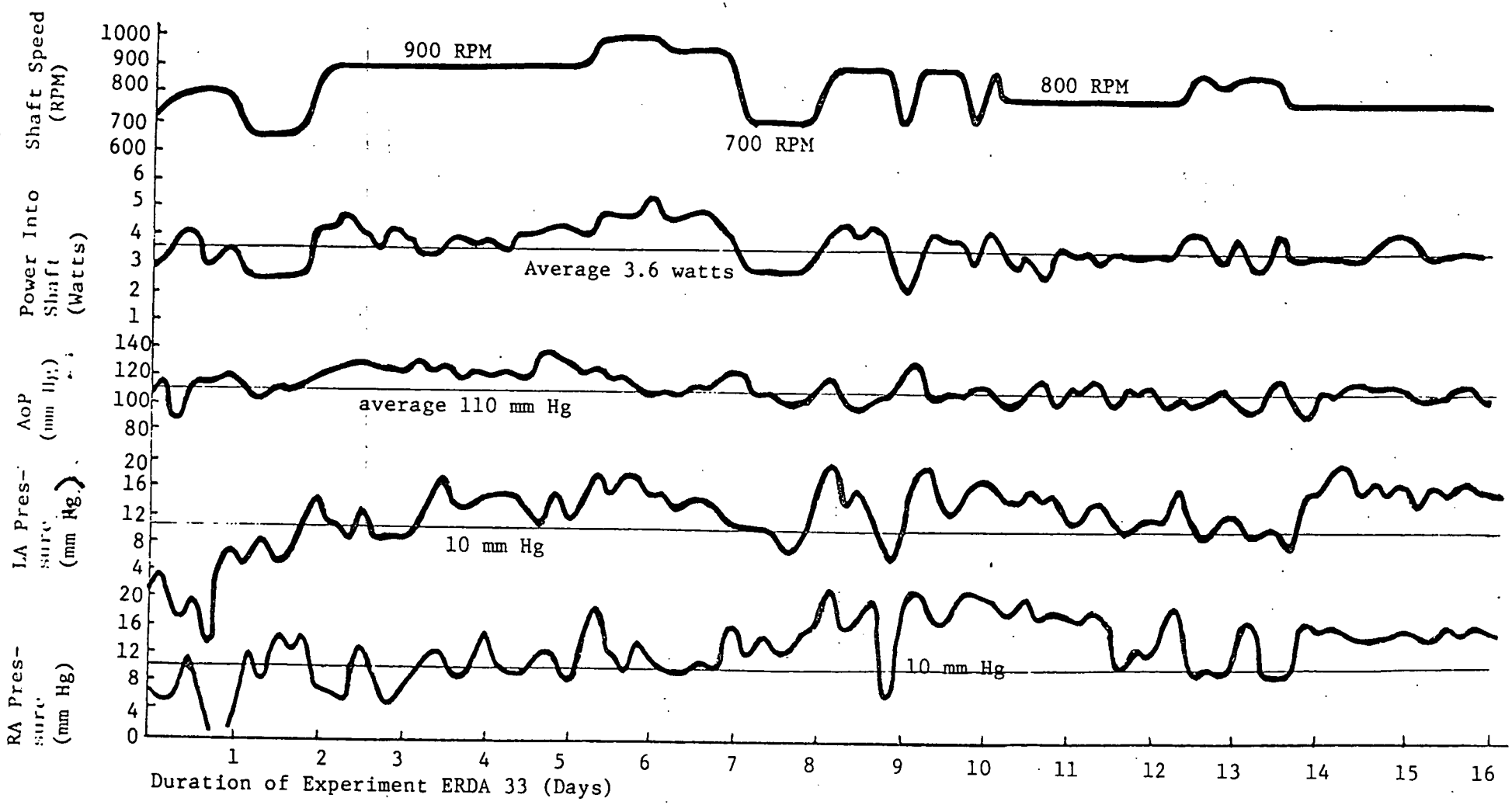
The natural outflow valves were successfully salvaged and cardiopulmonary bypass time was two hours and 17 minutes. Left and right atrial pressures, right ventricular pressure, aortic pressure and pulmonary arterial pressure were all monitored.

Postoperative Recovery:

The calf appeared to tolerate the surgery quite well and was standing within eight hours after implantation. Both left and right atrial pressures were low (LAP ranged from 0 to 5 mm Hg and RAP from 0 to 8 mm Hg) during the first day, indicating reasonable balance between left and right ventricular output. Blood pressures for the first day after surgery were about 0 mm Hg for the LAP, 6 mm Hg for the RAP and 55 mm Hg maximum for the RVP and 150 mm Hg maximum for the LVP. Mean torque to the pump was about 6 oz. inches. During the second day postoperative period the calf stood five different times for about five minutes each. For the second day, mean blood pressures were as follows: LAP at 6 mm Hg, RAP at 10 mm Hg and AoP at 130 mm Hg. Mean RPM was 700 r.p.m. and torque was 7 oz.-inches. During the third day the calf stood three different times. A pneumothorax was suspected and 400 cc of air was removed from the right thorax. Mean blood pressures during the third day were LAP at 10 mm Hg, RAP at 7 mm Hg and a peak aortic pressure of 160 mm Hg. Mean RPM was 900 r.p.m. and torque was 8 oz.-inches. On the fourth day a flouroscopic study was performed using lateral radiographs, which verified that the right pneumothorax had been corrected. The calf stood six different times, ate some grain and drank water. Mean blood pressures were RAP at 12 mm Hg, LAP at 14 mm Hg and aortic pressure of 145 mm Hg over 100 mm Hg. Mean speed for the blood pump remained at 900 r.p.m. and the average torque was 9 oz.-inches. During the fifth day the animal began to experience difficulty in standing, but did stand three different times.

After the 5th day the animal appeared to weaken and stood less, failing to stand unassisted after the 14th day. The animal exhibited some respiratory distress during the remaining survival period and was reintubated several times, as necessary. The animal did eat and drink throughout the experiment but the calf's appetite did abate somewhat in time. On the 16th day postoperative the calf could no longer be acceptably maintained and was terminated at 16 days and two hours after implantation of the ERDA blood pump with the ERDA II ventricles. Terminal mean circulatory blood pressures were 20 mm Hg.

The variation in time of the blood pressures, blood pump speed and power delivered to the pump during the 16.1 day survival period of the ERDA 33 experimental calf is shown in Figure XI-12. The average power consumed by the blood pump was 3.6 watts, which again confirms the previous observations that the use of the calf's own outflow valves significantly reduces power required by the blood pump. Mean aortic pressure was 110 mm Hg, which is near ideal for a calf, and the mean venous pressures (i.e. LAP and RAP) were both about 110 mm Hg, which is slightly high, but acceptable; and more significantly, their near equality implies that good progress towards balancing left and right ventricular outputs was achieved. Analysis made of the blood gases and their variation during the experiment is shown in Figure XI-13. The hematocrit progressively declined from an early value of 40% to a terminal value of about 25%. Both



FigureXI-12: Power Requirements and Blood Pressures for 16-Day ERDA Calf.

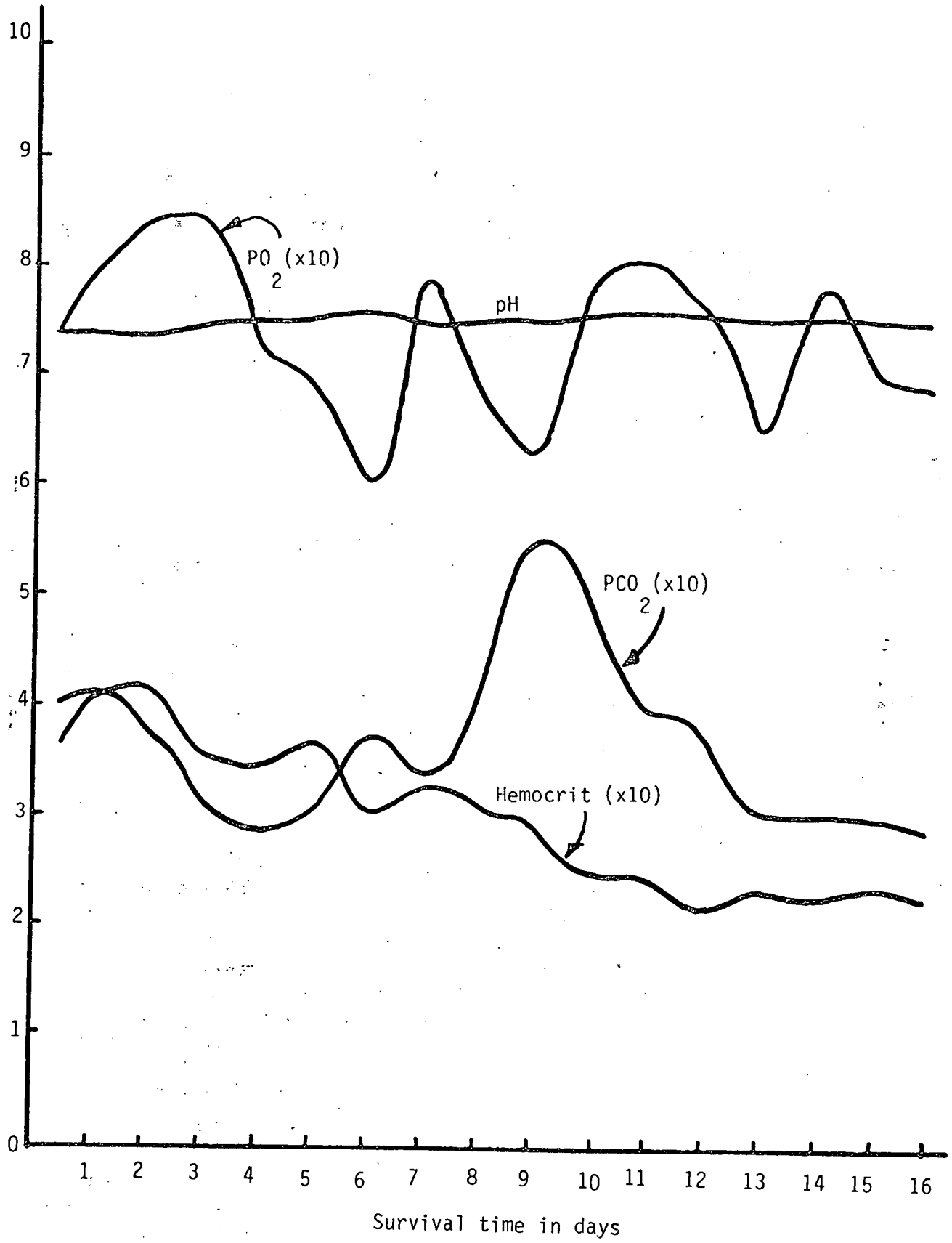


Figure XI-13. Variation of Blood Gases in Calf for ERDA Experiment No. 33.

Postoperative Recovery:

Immediately postoperatively the recovery was rapid, with the animal (named Charly) standing within a few hours. The calf was extubated at five hours without any respiratory complications. There were likewise no bleeding problems and the chest tubes were pulled at 23 hours. The postoperative course was uneventful, although left atrial and right atrial pressures went as high as 20 mm Hg for a short time, these high pressures were treated and corrected with diuretics.

On the 9th postoperative day Charly walked successfully on the treadmill. On the 10th day there was some drainage from the umbilical cord and it was thought that probably an abcess was developing around the electric motor. On the 14th day approximately 1-1/2 liters of pus and blood was drained from the abcess. A drain was put in at that time and the abcess cavity was irrigated with normal saline antibiotics. On the 17th day the motor speed controller failed, resulting in the motor running at very high speeds, producing a heart rate of approximately 200 beats/min. High aortic pressures and high torque was also noted at various times during this episode. An attempt was made to shift to a backup system but the connections were not interchangeable. After approximately one hour the shift was made to the backup motor controller by changing the cable at the umbilical cord. This brought the motor under control. Several minutes before shifting to the backup system the animal started to bleed very heavily from the drain in the abdominal abcess. This continued for several minutes and was finally treated by producing local pressure by closing the drain in the abcess, applying local pressure with bandages and also by giving massive blood transfusions.

Following these incidents the calf was weak but was able to stand, eat and drink. During the next 24 hours the bleeding continued until it was obvious that bleeding was out of control. At this time the animal was anesthetized and the tissue capsule containing the motor was opened to search for the source of bleeding. There was no bleeding from the capsule itself but blood was seen coming from the thorax along the drive shaft. An attempt was made to stop this flow of blood by tightly suturing tissue around the drive shaft. The capsule was then clotted with a drain in place. The calf recovered quickly and was extubated within an hour.

Post-surgically the calf continued to bleed and later went into shock, with an aortic mean pressure of 50. Subsequently the animal went into respiratory arrest and lost all reflexes. He was quickly intubated and fresh blood was given. Five hours post-respiratory arrest, the animal was standing, drinking and showed no neurological deficits. From the 19th to the 35th postoperative day the calf continued to be somewhat weaker than he had previously been, but was able to eat a little, drink, stand and was alert and attentive. During this period his nutrition was maintained by gavage feeding and liquid supplements. The abcess around the motor continued despite drainage, continuous flushing with normal saline and direct washing of the abcess cavity with Betadine solution.

On the 35th day the animal became less responsive, showed signs of septic shock and was anemic. During the 36th day the animal became progressively weaker and unresponsive to normal stimuli and was selectively terminated.

the pO_2 and pCO_2 varied during the experiment. The pO_2 of the arterial blood on room air during the post surgical period averages in the upper 60 mm Hg. The PA CO_2 should be 38 mm Hg. Peaking between the 8th to 11th day is not explainable but it returned to a normal level.

Autopsy Report:

At autopsy it was apparent that severe infection existed around the electric motor, along the power supply (umbilical cord), which penetrated the abdominal wall and even along the flexible drive shaft, which powers the blood pump. Bacteriologic cultures identified the presence of E. Coli, Enterobacter Aerogenes, Alcaligenes Faecalis and Staph Epidermidis. It was apparent that a sinus tract for transmission of infection was established from the penetration of the calf's skin over the right abdomen to the blood pump.

The blood pump appeared somewhat high and canted to the left, but the fit was good. The liver was enlarged and a mild pneumonia of the dependent portions of both lungs with atelectasis was evident. Echymosis over all lobes of the right kidney was found, with many small infected embolic infarcts evident. The assigned cause of death for the calf was the massive infection around the electric motor and blood pump and their connection lines, with sepsis and terminal septic emboli.

Summary of Total Artificial Heart Experiment No. 41 (TH77C2S27IIERDA41, IVBM8, January 11, 1977):

The primary objective of this experiment was to evaluate the IVBM blood pump with the new ERDA II style Silastic ventricles implanted, using a newly devised right thoracotomy protocol. The ventricles had been modified as follows: Right Ventricle: Regular outflow tract, 30 mil dome, reduced displacement volume (i.e. right pusher cup reduced in volume by 9.4%) and Bjork-Shiley inflow valve in No. 2 positions. Left Ventricle: Epoxy covered (for added rigidity) outflow tract, 30 mil dome, unmodified displacement volume and Bjork-Shiley inflow valve in No. 4 position. It was expected that with these modified ventricles (ERDA II ventricles) a balanced output between the left and right ventricle would be achieved. The calf's own natural pulmonary artery and aortic valves were used as outflow valves for the pump. ERDA Pump No. 8 was implanted with shaft No. W-132 and a vacuum drawn through the shaft casing and blood pump.

Surgical Procedure:

A 97.5 Kg female Holstein calf was selected for the experiment. The modified ERDA blood pump was implanted into the thorax via a right lateral thoracotomy surgical procedure. The natural outflow valves were successfully salvaged and cardiopulmonary bypass time was two hours 27 minutes. Left and right atrial pressures, right ventricular pressure, aortic pressure and pulmonary arterial pressure were all monitored.

Summary of Autopsy:

The following are positive findings:

1. PA outflow was too long and needed shortening by 2 cm.

2. Right atrium: fibrosis of cuff.

3. Left atrium: fibrosis of cuff.

4. Aortic valve: septic thrombus trained through valve from the graft. One cusp had perforation associated with kissing lesion.

5. Pressure lines: good tissue ingrowth.

6. Large thromboembolus in branch of PA plus numerous small hemorrhagic infarcts.

7. Liver: engorged with marked hemosiderosis and a large clot in a branch of the portal vein.

8. Kidneys: 2-3 older infarcts with multiple small to large abcesses.

9. Spleen: Hemorrhagic infarction of ventral 1/3.

10. Left ventrical housing: 1 cm tear in housing. Surrounding the artificial heart was stratified layer of new and old thrombus 4-8 cm thick. There were areas of very tough consolidated clots as well as areas of fresh clot.

11. Abcess surrounding electric motor.

12. Histopathology:

    A. Pathology secondary to septic thromboemboli.
    B. Lungs and liver: chronic passive congestion.

Conclusions:

This total heart experiment (ERDA 47 - Charly) was the most successful experiment to date. The animal stood within a few hours after surgery. Postoperative respiratory function was excellent with the animal being extubated five hours after surgery. Severe infection proximal to the motor was the primary cause of animal termination. Subsequent experiments would attempt to mitigate the infection tract produced by the bulky transcutaneous support lines to the electric motor. Some thromboembolism was apparent during autopsy but it was judged to be nonacute and controllable.

In Vivo Studies and Experiments

2. Summary of Total Artificial Heart Experiments Under the Contract

The Institute for Biomedical Engineering performed a total of 56 artificial heart implantation experiments in calves under the DOE Artificial Heart Contract. All these experiments employed the bench model or implantable version bench model (IVBM) blood pump which was driven by an electric motor directly attached or via a flexible drive shaft.

The first seven experiments used an externally located (not implanted within the calf) motor to power the blood pump, but problems with flexible shaft penetration through the chest wall dictated an early shift to internal implantation of the electrical motor within the abdominal wall of the calf. Because of local tissue heating problems attendent in the use of rather small inefficient electrical motors used for implantation, a water coolant jacket for the motor was designed and built. Experiments beginning with Experiment No. 10 to No. 53 used the coolant jacket with the implanted electrical motor and previous tissue damage due to local heating was eliminated. Experiments 54 through 56 used an electric motor attached to the blood pump. The early problems with flexible shaft failure encountered in experiments 1 through 9 were eliminated through the use of a heavier flexible shaft (3/16" diameter rather than 1/8" diameter) and a reinforced casing. No experiment suffered a shaft failure after experiment No. 9.

For the 56 total heart replacement experiments performed under this contract, the average survival time was 144 hours. The maximum survival time was 885 hours (35.9 days), which was ERDA Experiment No. 41, a very successful experiment. The calf in this experiment exhibited good overall physical and biological responses and was eating, drinking and able to stand and exercise on a treadmill throughout most of the experiment.

Table XI-1 provides a synopsis of all ERDA total heart replacement experiments performed by the Institute. Information categories with miscellaneous data appropriate to the goals of certain test series are given. Observe that since no failures in the flexible drive shaft were observed after Experiment No. 9, data on the drive shafts is not reported after Experiment No. 22. Instead, data on cardiopulmonary bypass (CPB) time, blood pump valves and power consumption are reported.

The mean CPB time for Experiments 23 through 56 was 162 minutes, with a standard deviation of 28 minutes. However, all of the experiments performed after experiment No. 32 preserved the animal's natural outflow heart valves which tended to lengthen CPB time. Mean time for those procedures in which natural valves were preserved was 168 minutes. Figure XI-14 presents a graph of animal survival times (on a logarithmic scale) in hours for each ERDA experiment. Mean animal survival time was 226 hours for Experiments 44 through 56 while the mean survival time for all animals that were not lost during surgery was 144 hours.

Figure XI-14 indicates the trend for increasing animal survival time, which is probably the best overall gross measure of in vivo performance of the DOE Artificial Heart System. A least squares curve fit for the survival data points is shown as a solid line in Figure XI-14. The equation for this line is as follows:

Expected survival = 22.1 (hours) exp. (.0469 x Experiment No.) with a correlation factor of $r^2 = 0.884$.

Figure XI-15 provides a graph of the probability of early failure, which is defined as an animal survival time of 10 hours or less for DOE artificial heart experiments. A survival time of 10 hours or less is assumed to be primarily due to early or immediate surgical errors or equipment malfunctions and are not believed to be an accurate indication of the DOE blood pump's capability and durability for serving as a heart replacement. The mean probability for early failure as established by the last few years of animal experiments with total heart replacement is 16% with a standard deviation of 2%. This value, though high, is not unreasonable or unexpected for such an ambitious program of developing a satisfactory total heart replacement system for man.

Finally, Figure XI-16 presents average power demands for the DOE blood pump in watts for selected DOE experiments. The mean power required to drive the blood pump with four prosthetic valves (which were Bjork-Shiley) was 5.6 watts, while the mean power required for two prosthetic and two natural outflow valves for each pump was only 3.7 watts. The conclusion reached here is that the prosthetic valves significantly decrease ventricular efficiency and raise the input power to the blood pump required to deliver adequate cardiac outputs.

TABLE XI-1

SYNOPSIS OF ERDA TOTAL HEART REPLACEMENT EXPERIMENTS

EXPERIMENT		SURVIVAL	TERMINATION	CALF	WANL	SHAFT CASING		FLEXIBLE SHAFT CORE	
NO.	DATE	HOURS	CAUSE	CONDITION	PUMP NO. AND MATERIAL	MATERIAL	LOCATION	SIZE & NO.	WINDING
1	6-12-73 C14 B13	10 min. on table	Shaft broke Kinked casing	On surgery table	#2 Silastic(S)	Nylon, Teflon-liner	External	1/8"Dx36" #1	Right
2	6-14-73 C15 B14	13 hours	Shaft broke	Under anesthesia	#2 Silastic(S)	Nylon, Teflon-liner	External	1/8"Dx36" #2	Right
3	8-2-73 C23 B22	11 hours	Shaft broke	Quiet - Stood at 9 hours	#2 Silastic(S)	Nylon, Teflon-liner	External	1/8"Dx36" #3	Right
4	8-30-73 C29 B26	13 hours	Shaft broke at chest entrance	Active-Tried to stand	#2 Silastic(R)	Nylon, Teflon-liner	External	1/8"Dx36" #4	Right
5	9-27-73 C35 B32	69 hours (2.9 days)	Severe sepsis sternum open	Active-Tried to stand	#2 Silastic(R)	Neoprene	External	1/8"Dx36" #5	Right
6	11-26-73 C43 B40	5 min.	Chest too small couldn't close chest-93 kg calf	On surgery table	#2 Silastic(R)	Neoprene	External	1/8"Dx36" #6	Right
7	12-11-73 C46 B43	25 hours (1 day)	Shaft broke near blood pump	Active-Tried to stand	#2 Silastic(R)	Neoprene	External	1/8"Dx36" #6	Right
8	1-10-74 C2 B2	5 min. on table	Quick connect-ventricle juncture broke	On surgery table	#2 Silastic(R)	Neoprene	Internal (small motor)	1/8"Dx8" #7	Left
9	2-14-74 C9 B9	36 hours (1.5 days)	Shaft broke	Active-Stood at 18 hours	#2 Silastic(R)	Neoprene	Internal	1/8"Dx8" #7	Left
10	5-29-74 C21 B21	14 hours	Suffocated, extubated accidently	Active-good condition, stood at 7 hours	#3 Silastic(R)	Neoprene	Internal (water cooled)	1/8"Dx6" #8	Right
11	6-10-74 C22 B22	44 hours (1.8 days)	Severe brain damage due to air embolis	Comatose	#3 Silastic(R)	Neoprene	Internal (water cooled)	1/8"Dx6" #9	Right
12	7-30-74 C28 B28	23 hours	Severe brain damage due to air embolis	Comatose	#3 Silastic(R)	Neoprene reinforced casing	Internal (water cooled)	1/8"Dx6" #10	Right

TABLE XI- 1 (Continued)

SYNOPSIS OF ERDA TOTAL HEART REPLACEMENT EXPERIMENTS
(Continued)

EXPERIMENT		SURVIVAL	TERMINATION	CALF	WANL	SHAFT CASING		FLEXIBLE SHAFT CORE	
NO.	DATE	HOURS	CAUSE	CONDITION	PUMP NO. AND MATERIAL	MATERIAL	LOCATION	SIZE & NO.	WINDING
13	8-5-74 C29 B29	0 on table	Blood pump malfunction	On surgery table	#3 Silastic(R)	Neoprene reinforced casing	Internal (water cooled)	1/8"Dx6" #11	Right
14*	8-16-74 C31 D31	87 hours (3.6 days)	Electrical motor mal-function	Fair	#2 Silastic(R)	Neoprene reinforced casing	Internal (water cooled)	1/8"Dx6" #12	Right
15*	11-21-74 C41 ERDA 15	100 hours (4.2 days)	Pulmonary failure	Active-Stood several times	#2 Silastic(R)	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #13	Right
16*	2-11-75 C6 A1	28 hours (1.2 days)	Blood pump Alignment	Fair	#2 Avcothane #1	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #14	Right
17	4-8-75 C12 A3	266 hours (11.1 days)	Cerebral stroke	Good-Stood several times	#2 Avcothane #1	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #15	Right
18	5-29-75 C14 ERDA 18	5 min.	Malfunction of electric motor for blood pump	On surgery table	#2 Avcothane #2	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #16	Right
19	6-18-75 C16 A4	50 hours (2.1 days)	Pulmonary failure	Fair	#2 Avcothane #2	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #17	Right
20	7-17-75 C20 A5	10 min.	Blood pump ventricle leakage	On surgery table	#2 Avcothane #3	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #18	Right
21	7-29-75 C21-ERDA 21	121 hours (5.0 days)	Pulmonary failure	Good-Stood several times	#2 Avcothane #3	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #19	Right
22	8-13-75 C23 ERDA 22	507 hours (21.1 days)	Bleeding Diathesis	Excellent-Stood often-placed on treadmill	#2 Silastic(R)	Neoprene reinforced casing	Internal (water cooled)	3/16"Dx6" #20	Right

*Chest reopened to correct internal bleeding.

TABLE XI-1 (Continued)

SYNOPSIS OF ERDA TOTAL HEART REPLACEMENT EXPERIMENTS

EXPERIMENT NO.	DATE	SURVIVAL TIME	TERMINATION CAUSE	CALF CONDITION	PUMP NO. & MATERIAL	BYPASS TIME	VALVE NO. & TYPE	MEAN POWER CONSUMPTION
23	11-4-75 C21 S12	68 hours (2.8 days)	Pulmonary failure	Good, stood several times	No. 4: IVBM oil filled, Silastic	176 min	4 Bjork-Shiley (BS)	4.7 watts @ 900 rpm
24	11-14-75 C33 S11	83 hours (13.5 days)	Pulmonary failure and hemorrhage near quick connect	Fair	No. 4: IVBM oil filled, Silastic, Dacron fibrils	116 min	4 (BS)	4.3 watts @ 950 rpm
25	12-11-75 C35 A4	2 hours	Excess bleeding through left atrial cuff	Died on surgery table	No. 3: bench model, Avcothane, smooth	137 min	4 (BS)	--
26	1-6-76 C36 S14	2 hours	Malfunction of electric motor for blood pump	Died on surgery table	No. 3: bench, Silastic, smooth	---	4 (BS)	--
27	1-20-76 C1 S15	20 hours	Pulmonary edema	Good	No. 3: bench, Silastic silicon dispersion coating	125 min	RA & LA (BS) RV & LV Natural (Nat)	2.8 watts @ 600 rpm
28	1-29-76 C2 S15	53 hours (2.2 days)	Pulmonary failure	Fair. Animal had pneumonia	No. 4: IVBM oil filled	137 min	4 (BS)	2.2 watts @ 600 rpm
29	2-5-76 C3 S16	131 hours (5.5 days)	Pulmonary failure	Good.	No. 3: Bench	183 min	RA & LA (BS) RV & LV (Nat)	3.0 watts @ 600 rpm
30	2-19-76 C4 S17	99 hours (4.1 days)	Electric motor malfunction	Fair. Animal fibrillated during surgery	No. 4: IVBM oil filled Silastic silicone dispersion	168 min	RA & LA (BS) RV & LV (Nat)	3.2 watts @ 750 rpm
31	4-9-76 C5 S18	29 hours (1.2 days)	Pulmonary failure	Fair		77 min	4 (BS)	4.9 watts @ 900 rpm
32	4-23-76 C7 S18x2	162 hours (6.8 days)	Electric motor malfunction	Good	No. 4: Silastic silicone dispersion coated	141 min	RA & LA (BS) RV & LV (Nat)	4.4 watts @ 800 rpm
33	7-13-76 C11 521 II	368 hours (16.1 days)	Infection	Good	No. 8: Modified ERDA II Silastic	137 min	RA & LA (BS) RV & LV (Nat)	3.8 watts @ 800 rpm

TABLE XI-1 (Continued)

SYNOPSIS OF ERDA TOTAL HEART REPLACEMENT EXPERIMENTS

EXPERIMENT NO.	DATE	SURVIVAL TIME	TERMINATION CAUSE	CALF CONDITION	PUMP NO. & MATERIAL	BYPASS TIME	VALVE NO. & TYPE	MEAN POWER CONSUMPTION
34	8-31-76 C14 S22II (98 Kg)	0 on table	Leakage in LV outflow tract produced air embolism	Died on surgery table	No. 7 ΔV modified ERDA II Silastic	148 min.	RA & LA (BS) RV & LV (nat)	----
35	9-2-76 C15 S22II (99 Kg)	42 hours (1.8 days)	Blood leakage thru tear in diaphragm, resulting in electrical overload	Fair, stood several times	No. 7 ΔV modified ERDA II Silastic	144 min.	RA & LA (BS) RV & LV (nat)	5.0 watts @ 800 RPM
36	9-6-76 C17 S23II (109 Kg)	42 hours (1.8 days)	Broken, flexible overload drive shaft due to pump overload	Fair, stood several times	No. 7 ΔV modified ERDA II Silastic	160 min.	RA & LA (BS) RV & LV (nat)	4.3 watts @ 800 RPM
37	11-2-76 C21 S24II (111 Kg)	40 hours (1.7 days)	Pulmonary failure, mechanical failure, oxygenator	Poor, stood twice	No. 7 ΔV modified ERDA II Silastic	148 min.	RA & LA (BS) RV & LV (nat)	4.1 watts @ 800 RPM
38	11-11-76 C23 S25II (105 Kg)	102 hours (4.3 days)	Thrombosis & thromboemboli (possibly pneumonia)	Good, stood several times	No. 8 ΔV modified ERDA II Silastic	173 min.	RA & LA (BS) RV & LV (nat)	4.2 watts @ 750 RPM
39	12-7-76 C25 S1I (100 Kg)	93 hours (3.9 days)	Pulmonary failure	Poor, didn't stand	No. 7 ΔV modified ERDA II Silastic	188 min.	RA & LA (BS) RV & LV (nat)	4.1 watts @ 750 RPM
40	12-21-76 C26 S II (109 Kg)	94 hours (4.0 days)	Pulmonary failure	Poor, lungs damaged	No. 8 ΔV modified ERDA II Silastic	183 min.	RA & LA (BS) RV & LV (nat)	4.2 watts @ 800 RPM
41	1-11-77 C2 S27II (105 Kg)	885 hours (36.9 days)	Infection & thrombo-embolism	Excellent. Stood, exercised, ate and drank	No. 8 ΔV modified ERDA II Silastic	147 min.	RA & LA (BS) RV & LV (nat)	5.0 watts @ 900 RPM

TABLE XI-1 (Continued)

SYNOPSIS OF ERDA TOTAL HEART REPLACEMENT EXPERIMENTS

EXPERIMENT NO.	DATE	SURVIVAL TIME	TERMINATION CAUSE	CALF CONDITION	PUMP NO. & MATERIAL	BYPASS TIME	VALVE NO. & TYPE	MEAN POWER CONSUMPTION
51	8-22-77 C22 S35 II (116 Kg)	33 hours (1.4 days)	Pulmonary failure Pulmonary edema in both lungs	Poor, never stood.	No. 8 ΔV modified ERDA II Silastic	185 min.	RA & LA (BS) RV & LV (nat)	No torque measurements. Mean speed: 900 RPM
52	9-15-77 C23 S36 II (120 Kg)	266 hours (11.1 days)	Pulmonary failure. Pulmonary Edema in both lungs.	Fair, stood many times. Condition deteriorated after 7th day.	No. 8 ΔV modified ERDA II Silastic with anticipated switch to IVBM thermal converter.	180 min.	RA & LA (BS) RV & LV (nat)	No torque measurements. Mean speed: 1000 RPM
53	10-11-77 C26 S37 II (100 Kg)	215 hours (9 days)	Pulmonary failure. Pulmonary infection evident	Fair, stood several times	No. 8 ΔV modified ERDA II Silastic	168 Min.	RA & LA (BS) RV & LV (nat)	No torque measurements. Mean speed: 1000 RPM
54	12-9-77 C31 S II (128 Kg)	269 hours (11.2 days)	Mechanical failure. Blood pump speed controller erratic	Good, stood many times, ate and drank, exercised	No. 8 ΔV modified ERDA II Silastic. Electric motor attached to blood pump	179 min.	RA & LA (BS) RV & LV (nat)	No torque measurements. Blood pump mean rate: 122 BPM, standard deviation 16 BPM
55	3-14-78 C7 S II (129 Kg)	330 hours (13.8 days)	Electrical power leads broke	Good	No. 8 ΔV modified ERDA II Silastic. Electric motor attached to blood pump	157 min.	RA & LA (BS) RV & LB (nat)	No torque measurements. Blood pump mean rate: 122 BPM, standard deviation 16 BPM
56	4-14-78	121 hours (5.0 days)	Pulmonary failure, terminated	Good	No. 8 ΔV modified ERDA II Silastic Electric motor attached to blood pump	157 min.	RA & LA (BS) RV & LB (nat)	No torque measurements. Blood pump mean rate: 122 BPM, standard deviation 16 BPM

TABLE XI-1 (Continued)

SYNOPSIS OF ERDA TOTAL HEART REPLACEMENT EXPERIMENTS

EXPERIMENT NO.	DATE	SURVIVAL TIME	TERMINATION CAUSE	CALF CONDITION	PUMP NO. & MATERIAL	BYPASS TIME	VALVE NO. & TYPE	MEAN POWER CONSUMPTION
42	1-26-77 C3 S28 II (117 Kg)	93 hours (3.9 days)	Pulmonary failure	Good, stood several times	No. 7 ΔV modified ERDA II Silastic	178 min.	RA & LA (BS) RV & LV (nat)	4.3 watts @ 800 RPM
43	2-24-77 C5 S28 II (103 Kg)	92 hours (3.8 days)	Thromboemboli from ventricles	Good, stood seven times	No. 7 ΔV modified ERDA II Silastic	155 min.	RA & LA (BS) RV & LV (nat)	4.2 watts @ 850 RPM
44	3-8-77 C6 S29 II (104 Kg)	194 hours (8.1 days)	Hypotension and equipment failure	Fair, stood twice	No. 7 ΔV modified ERDA II Silastic	197 min.	RA & LA (BS) RV & LV (nat)	4.5 watts @ 900 RPM
45	4-7-77 C9 S30 II (101 Kg)	315 hours (13.1 days)	Pulmonary failure and severe infection	Fair, did not stand	No. 7 ΔV modified ERDA II Silastic	185 min.	RA & LA (BS) RV & LV (nat)	4.4 watts @ 900 RPM
46	5-10-77 (105 Kg)	0 hours. Thermal converter fit trial	Fit trial revealed that thermal converter required placement in peritoneum for accomodation		No. 7 ΔV modified ERDA II Silastic	- 0 -	None	None
C47	5-19-77 C12 S31 II (103 Kg)	368 hours (15.3 days)	Mechanical failure, flexible shaft broke	Fair, did not stand	No. 7 ΔV modified ERDA II Silastic	161 min.	RA, LA & LV (BS), RV (nat)	4.6 watts @ 800 RPM
48	6-16-77 C14 S32 II (127 Kg)	25 hours (1 day)	Failure of thermal converter resulted in long bypass time neurological failure, pneumothorax	Poor, brain damage	No. 7 ΔV modified ERDA II Silastic	209 min.	RA & LA (BS) RV & LV (nat)	No torque measurements @ 850 RPM
49	7-12-77 C17 BICH 1 (108 Kg)	16.3 hours (.68 day)	Pulmonary failure	Poor, never recovered from surgery	No. 7 ΔV modified ERDA II Silastic	195 min.	RA & LA (BS) RV & LV (nat)	No torque measurements @ 900 RPM
50	8-9-77 C20 S34 II (105 Kg)	560 hours (23.3 days)	Mechanical failure. Shear pin broke in blood pump.	Excellent, stood more than 150 times, ate and drank, exercised on treadmill	No. 7 ΔV modified ERDA II Silastic	149 min.	RA & LA (BS) RV & LV (nat)	4.5 watts @ 1000 RPM

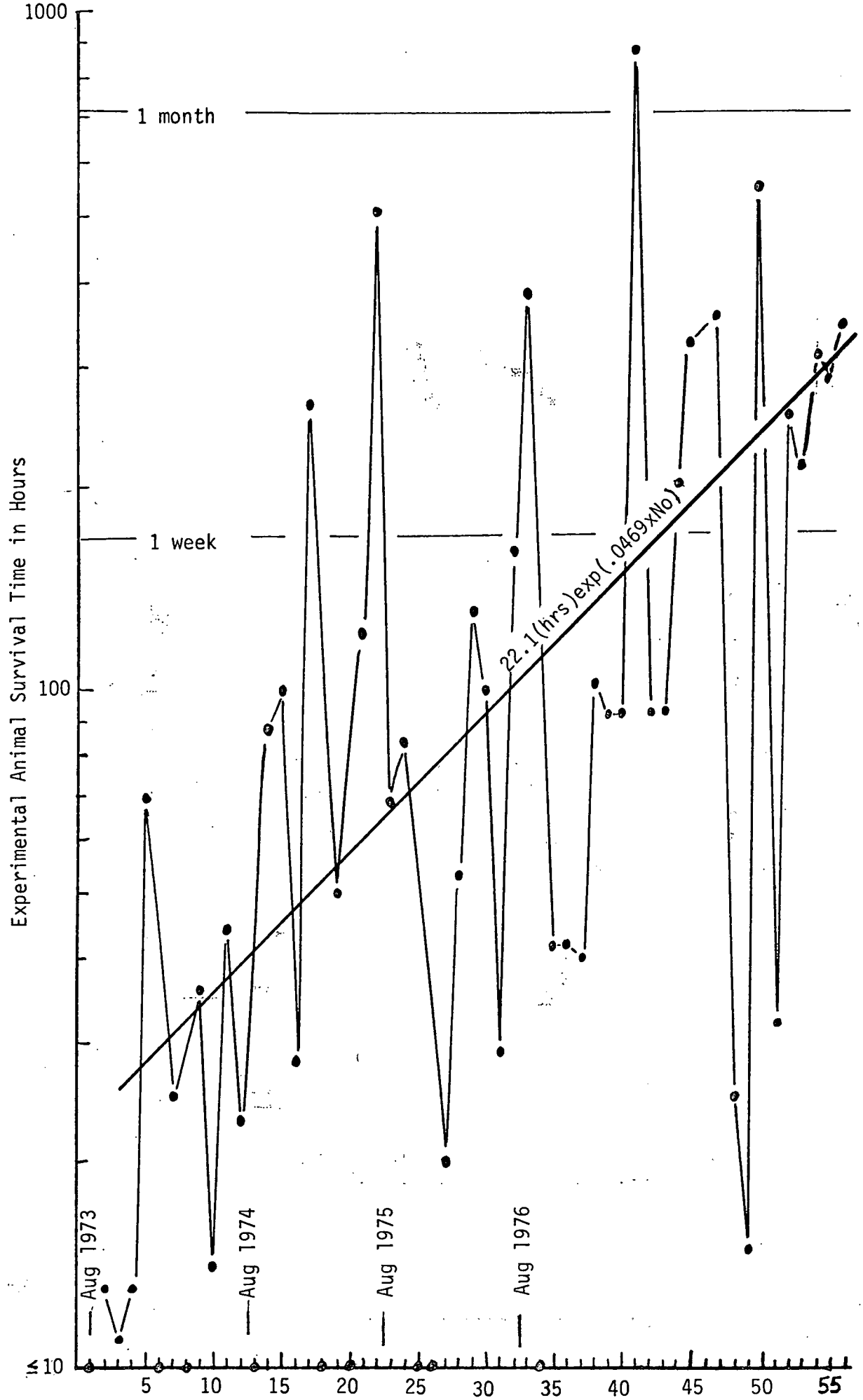


Figure XI-14: ERDA Total Artificial Heart Experiment Number

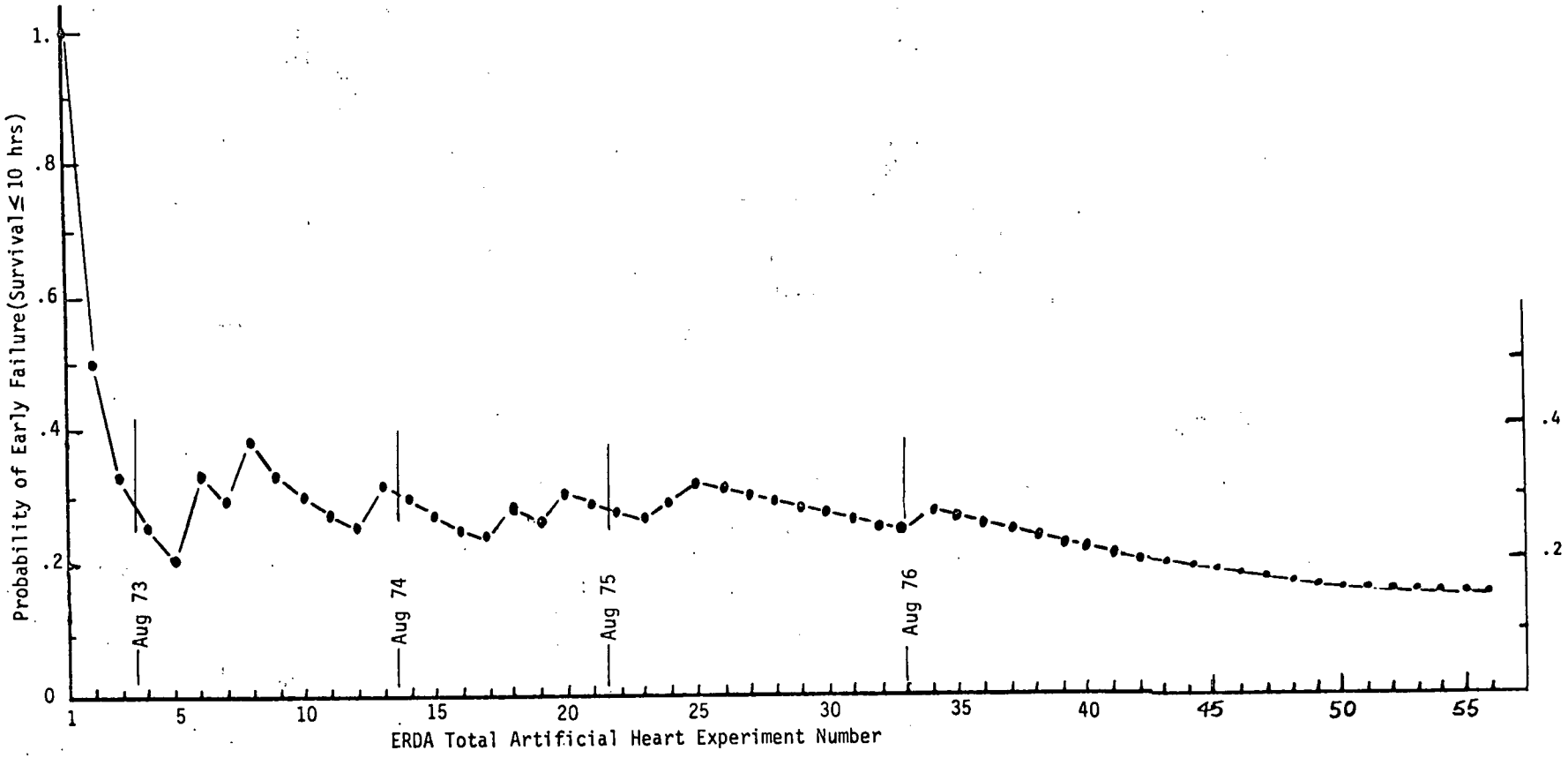


Figure XI-15. Probability of early failure (survival $\leq$ 10 hours) of ERDA Artificial Heart Experiment.

Average Power Requirements For ERDA Mechanical Blood Pump

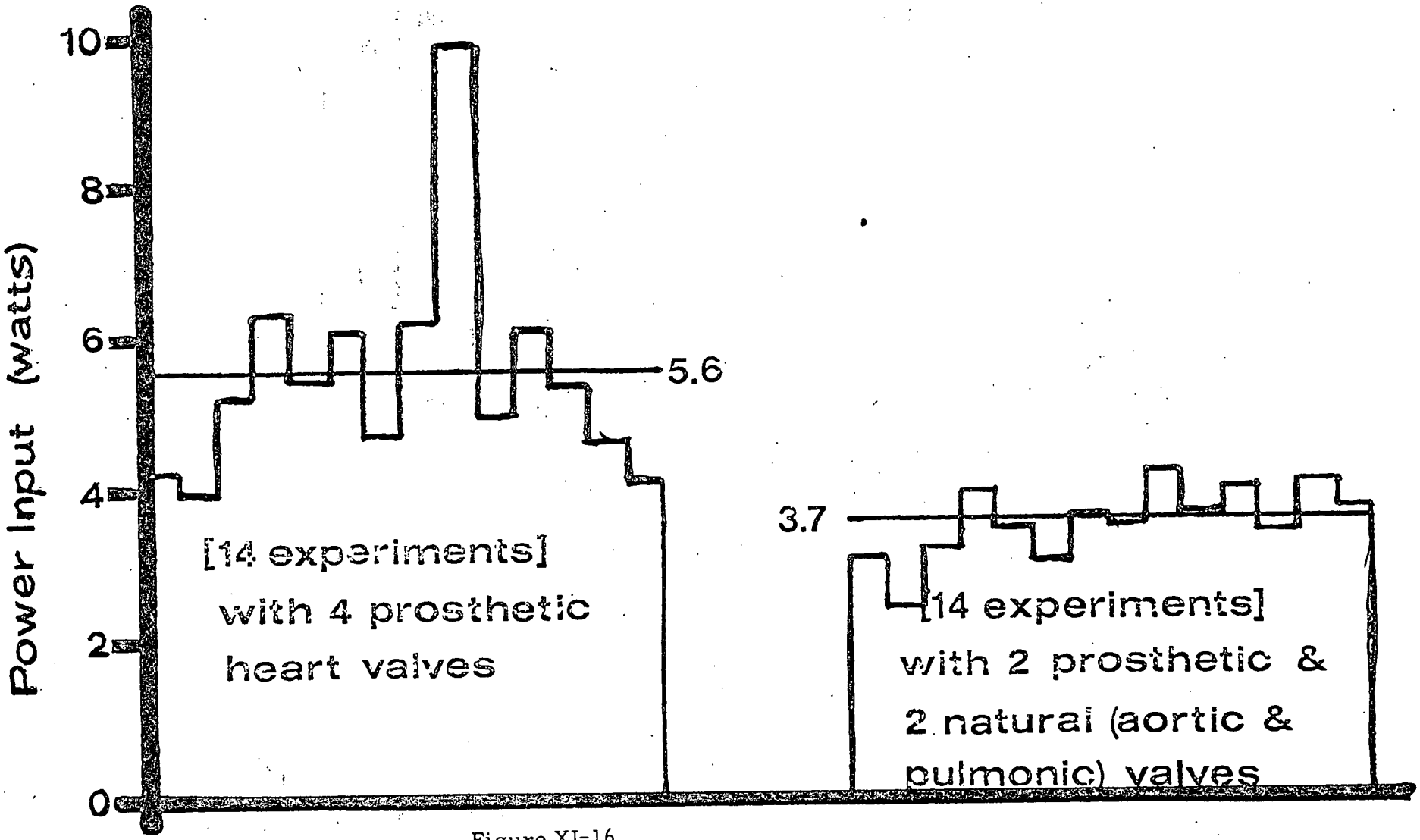


Figure XI-16

Preparation of Surgical Protocol

A complete surgical protocol for Total Heart Replacement with the Blood Pump and implanted electrical motor drive was developed and repetitively tested and evaluated. The following is a sample protocol used on Experiment Number 57 on May 4, 1978. A related protocol for follow-up surgery entailing replacement of the electrical motor with the IVBM Thermal Converter is also shoen. However, the Thermal Converter could not be operated successfully during the trial experiment, and the Thermal Converter was not implanted in an experimental animal.

Protocol

DOE TOTAL HEART REPLACEMENT

TH77 C23 SII36 DOE 52

DATE: THURSDAY, September 15, 1977

PRINCIPAL INVESTIGATOR:

PURPOSE OF EXPERIMENT:

Short-term evaluation of the air-filled IVBM blood pump powered by the electrically heated thermal converter. Two stage implantation: Phase I is electrical motor implantation; Phase 2 exchange of electric motor for thermal converter.

HEART:

RVP and LAP taps only. (RFGD) 5 minute @ 50 watts.
Smooth Silastic, Type II design, with felt cuffs.
Right Ventricle: 8.4% ΔV pusher cup. Inflow valve #2 position.
Left Ventricle: 0% ΔV with epoxy snout. Inflow valve #4 position.

1ST STAGE DRIVING SYSTEM: Wertronix electric motor #105 with controller #105 oil mode. Drive shaft #WI47 velour covered.

2ND STAGE DRIVING SYSTEM: IVBM, electrically heated thermal engine.

ANIMAL: Calf, approximately 127 Kg.

PERSONNEL:

Surgeons:
Recording and Log:
Pressure Recording:
Anesthesia:
Instruments:
Oxygenator:
Electrical Motor/Thermal Engine Exchange:
Circulating:
Hematology:

ANESTHESIA: Brevane induction, followed by fluothane.

MONITORING:

Pressures: continuously RVP 0-80 mm Hg, continuously LAP 0-20 mm Hg.
During Surgery: Femoral pressures and CVP. Lines removed after surgery.

Phase I: Electric Motor: Speed 0-1.5 V/10 div., torque 0-2.4 V/8 div.

Phase II: Thermal Converter: Recording only buffer pressure. Intermittent recording of hot and cold engine temperature, as necessary.

LAB PACK: As for total heart DOE, plus extra sterile clothes and Betadyne solution for wiping up excess sperm oil during exchange of electric motor with thermal converter.

PREOPERATIVE:

1. Tuesday Sept. 13, initiate start-up procedures for the thermal converter (see thermal converter protocol, Section 3.2.2).
2. Confine calf to cage for 24 hours, NPO for 24 hours, no water for 12 hours.
3. Lung function studies 24 hours preop.
4. Clip and prep animal just prior to experiment or night before.
5. Neomycin 2000 mg 8 hrs preop.
6. Coupling mechanism is attached to pump (both are oil filled). Coolant lines are filled with water and capped. Nose cone and thermal insulation in place.
7. Hematology workup.

OPERATIVE PROCEDURES:

FIRST STAGE

1. Blood samples for lab, A.C.T.
2. Induce with brevane and 2.0 mg atropine. Place calf on left side. Place rubber mat under animal.
3. Intubate and connect to respirator.
4. Repeat blood gases determination during operation.
5. Prep and drape to insert pressure lines in left saphenous vessels.
6. Expose the right jugular vein and carotid artery.
7. Right thoracotomy.
8. Dissect and place tourniquets on SVC and IVC azygous vein. Open the pleural sac containing the intermediate lobe of the lung.

9. Open pericardium, dissect and place tourniquets on aorta, preclot grafts.
10. Tunnel subcutaneously for placement of drive lines, motor, shaft etc.
11. Heparinize with standard dose, 5 mg/Kg.
12. Place bypass lines, arterial line in carotid.
13. Start partial bypass very slowly, not more than 0.5 L/min. Stay on partial bypass for at least three minutes to get adequate mixture of blood and priming solution.
14. Total bypass. Ligate hemiazygos vein and excise ventricles, leaving the PA and Ao valves.
15. Maintain PEEP 5 cm H_2O on lungs during bypass.
16. Suture both left atrial cuff and aortic graft to trigonium. Finish aortic graft and then the left cuff.
17. Suture the right cuff.
18. Suture PA graft.
19. Insert blood pump through chest wall and insert pressure catheters. Install electric motor in abdomen.
20. Prime ventricles with saline.
21. Connect bypass and place chest drains.
22. Stop bypass and place chest drains.
23. Check for leaks, remove bypass lines and start protamine sulfate to return A.C.T. to control value.
24. Close chest, repair jugular vein and carotid artery. Remove femoral artery line. Remove CVP line 12 hours post.

SECOND STAGE: Thermal Converter Implantation

PREOPERATIVE PROCEDURE:

The thermal converter has been sterilized and is running in a sterile chamber with the auxiliary coolant system operating, and a starter motor connected to the flywheel end.

Anesthetize and intubate and surgically prep the animal.

OPERATIVE:

1. Incise through former abdominal incision and expose the electric motor.
2. Examine site and prepare for thermal converter as required.
3. Heparinize.
4. Remove operating thermal converter, starting cradle and auxiliary lines from the sterile chamber and attach to sterile sling.
5. Remove output shaft closure from thermal converter and maneuver cradle and sling to place converter over abdomen alongside incision.
6. Remove blood pump electric motor from incision and place on abdomen.

7. Peel back Silastic from flexible shaft ferrule and unscrew ferrule, maintaining connection between blood pump motor and shaft manually.
8. Stop blood pump motor and stall converter with converter starter motor. Disengage starter motor from thermal converter by retracting starter motor longitudinally along positioning track. Remove blood pump motor from flexible shaft.
9. Connect thermal converter to flexible shaft. After flexible shaft connection is made, engage starter motor with thermal converter by advancing it longitudinally along positioning track. Adjust thermal converter in holding bracket to secure alignment between flywheel shaft and motor shaft if necessary.
10. Start thermal converter with auxiliaries connected by energizing starter motor.
11. With oil-filled syringe, engage bleeding port on gear box and charge with sperm oil and remove air creating mild vacuum.
12. Check thermal converter for normal, stable operation.
13. Monitor blood pressures and thermal converter temperatures.
14. Remove starter shaft and cap off fitting.
15. Check thermal converter for normal operation.
16. Disconnect instrumentation leads from auxiliary cart, attach protective covering over leads.
17. Remove the thermal converter from cradle and place thermal converter in abdominal cavity or peritoneal cavity and route instrumentation lines through existing skin tunnel.
18. Close abdominal incision and re-connect instrumentation leads to auxiliary cart.
19. Place calf in cage.
20. Initiate chest drain vacuum.
21. Initiate recovery procedure, normothermia, and lung ventillation as dictated by blood gases.

POSTOPERATIVE:

1. Monitor hot finger temperatures and working pressure as described on appropriate procedure.
2. Antibiotics: Penicillin 20 million U in pump.
3. Respiratory: Keep venous P^{O}_{2} above 30, occasional PEEP, extubate when possible.
4. Blood transfusions: Maintain hematocrit above 30% for the first 48 hours.

NOTE: Change trachea tube every 24 hours. If there are any changes, please contact Principal Investigator.

In Vivo Studies and Experiments

Development of Pulmonary Function Testing Technique

A simple method of measuring the lung functions and residual capacity of experimental animals was developed. This technique served a twofold purpose:

1. To serve as a screening device for preoperative lung evaluations of calves.
2. To monitor on a routine basis the respirator capabilities of the calves after surgery while they are maintained with the AEC Blood Pump.

The testing equipment utilized (see Figure XI-17) a Warren E. Collins residual volume and diffusion study spirometer console. Associated with this equipment, a protocol was developed for properly using the equipment on a pre and post operative basis, along with a work sheet to facilitate calculating lung function studies (see Table XI-2.).

This testing procedure was employed on a large number of calves and permitted the development of normal values based on a calf with an average weight of 95 kg.

Normal values for a 95 kg Holstein calf are:

1. Minute volume: 28 ± 4 Liters/minute
2. Respiratory rate: 44 ± 10 Breaths/minute
3. Tidal volume: 700 ± 100 Liters/breath
4. Oxygen uptake: 545 ± 50 cc/minute
5. Functional residual capacity: $4{,}800 \pm 500$ cc.

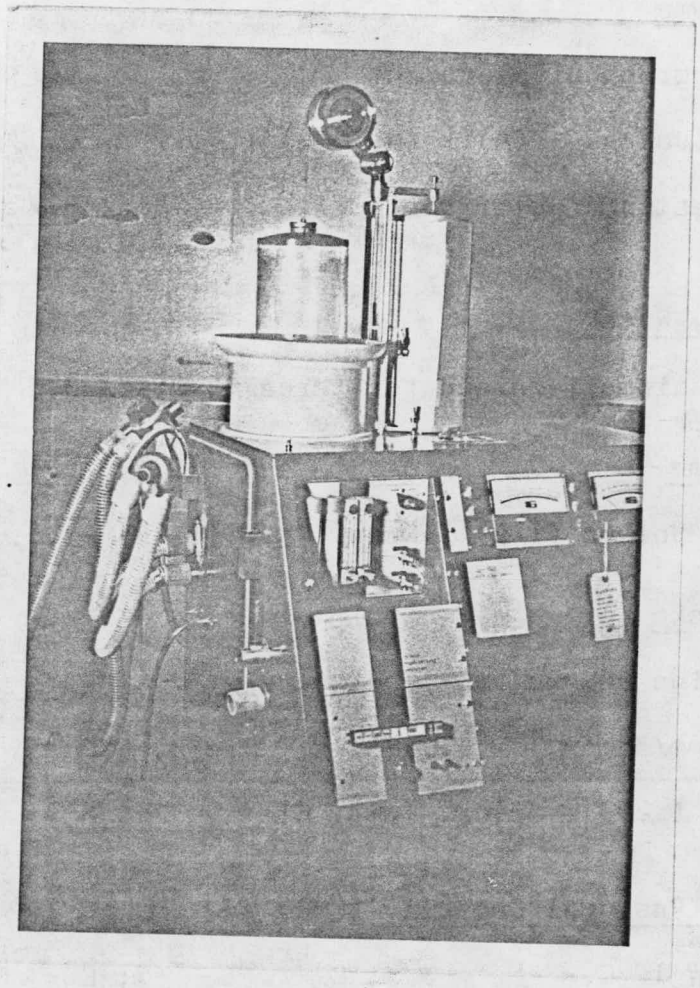


Fig.XI-17 Pulmonary function equipment for pre and postoperative measurements. W.E. Collins Spirometer.

Table XI-2:

Department of Artificial Organs

PULMONARY FUNCTION TESTS

Work Sheet for Spirometry

Calf No._____ Date_____ Weight_____Kg.

Pre-Op._____ Post-Op._____/_____Hrs. Standing_____ Sitting_____

Person conducting test_____ Temp._____C° Press._____mmHg

I. Minute Volume

A. Ventilograph displacement _____mm/3 min.

B. Minute volume = (A) x (0.1884)* =.....(BTPS) _____ - _____ L/min

* Correction factor (0.1884) = $\frac{(20.73\text{cc/mm} \times \text{Vent. Fact.}(25) \times 1.093)}{(3.0 \text{ min.} \times 1000 \text{ cc/L})}$

II. Respiratory Rate

A. Respirations recorded for three minutes/ 3.0 = ... _____ Resp/min

III. Tidal Volume

A. Minute Volume (I-B) / Resp. Rate (II-A) = ...(BTPS)_____ L/Breath

IV. Oxygen Uptake

A. Base line change for 3. minutes = _____mm.

B. $\frac{(\text{IV-A mm/3 min.}) \times (2.475) \times (\text{Press.}-47\text{mmHg.}\_\_\_\_\_)}{(273 + \text{Spior. Temp. C°}\_\_\_\_\_\text{K°})} = \frac{\_\_\_\_\_ \text{cc.}}{\text{(STPD)} \quad \text{min}}$

V. Functional Residual Capacity (FRC)

A. Trial # 1 C_1=_____%; C_2=_____%; C_3=_____%

Volume of Air added = Vol. A. = _____L.

Switch Error =Sw.Er. = _____cc. ($\bar{+}$)

B. Trial # 2 C_1=_____%; C_2=_____%; C_3=_____%

Vol. A. =_____L. ; Sw. Er.=_____cc. ($\bar{+}$)

C.

$$\text{FRC (BTPS)} = \left((C_1 \,/\!/\, C_3) \times \frac{(C_2 - C_3)}{(C_1 - C_2)} \times (\text{Vol. A.}) \times 1.093 \right) - 300\text{cc.} + (\text{Sw. Er.})$$

FRC (trial #1).....(BTPS)_____cc.

FRC (trial #2).....(BTPS)_____cc.

LMS-10/73

APPENDIX NO. 1

Documents Submitted Under This Contract

COO-AT(11-1)-2155-1
Quarterly Progress Report (6/15/71 to 9/15/71)

COO-AT(11-1)-2155-2
Quarterly Progress Report (9/15/71 to 12/15/71)

COO-AT(11-1)-2155-3
Quarterly Progress Report (12/15/71 to 3/15/72)

COO-AT(11-1)-2155-4
Quarterly Progress Report (3/15/72 to 6/15/72)

COO-AT(11-1)2155-5
Annual Report (6/15/71 to 7/15/72)

COO-AT(11-1)-2155-6
Quarterly Progress Report (7/15/72 to 10/15/72)

COO-AT(11-1)-2155-7
Quarterly Progress Report (10/15/72 to 2/15/73)

COO-AT(11-1)-2155-8
Quarterly Progress Report (2/16/73 to 5/15/73)

COO-AT(11-1)-2155-9
Annual Report (7/15/72 to 8/14/73)

COO-AT(11-1)-2155-10
Quarterly Progress Report (8/16/73 to 11/15/73)

COO-AT(11-1)-2155-11
Quarterly Progress Report (11/15/73 to 2/14/74)

COO-AT(11-1)-2155-12
Quarterly Progress Report (2/15/74 to 5/14/74)

COO-AT(11-1)-2155-13
Annual Report (7/15/73 to 8/15/74)

COO-AT(11-1)-2155-14
Quarterly Progress Report (8/16/74 to 11/15/74)

COO-E(11-1)-2155-15
Quarterly Progress Report (11/16/74 to 2/15/75)

Appendix 1 (Continued)

COO-E(11-1)-2155-17
Quarterly Progress Report (2/14/75 to 5/15/75)

COO-E(11-1)-2155-18
Quarterly Progress Report (5/16/75 to 8/14/75)

COO-EY-76-2155-19
Annual Progress Report (8/15/75 to 8/14/76)

COO-EY-76-2155-20
Progress Report (8/15/76 to 5/15/77)

COO-EY-78-2155-21
Final Report (6/15/71 to 6/31/79)

Appendix 1 (Continued)

Backman, D.K.; Donovan, F.M.; Sandquist, G.; Kessler, T. and Kolff, W.J. The Design and Evaluation of Ventricles for the AEC Artificial Heart Nuclear Power Source. Abst. Amer. Soc. Artif. Int. Organs, Vol. 2, 1973.

Backman, D.B.; Donovan, F.M.; Sandquist, G.; Kessler, T. and Kolff, W.J. The Design and Evaluation of Ventricles for the AEC Artificial Heart Nuclear Power Source. Trans. Amer. Soc. Artif. Int. Organs, 19:542-552, 1973.

Smith, L.; Backman, K.; Sandquist, G. and Kolff, W.J. Development on the Implantation of a Total Nuclear-Powered Artificial Heart System. Abst. Amer. Soc. Artif. Int. Organs, Vol. 3, 1974.

Smith, L.; Backman, K.; Sandquist, G. and Kolff, W.J. Development on the Implantation of a Total Nuclear-Powered Artificial Heart System. Trans. Amer. Soc. Artif. Int. Organs, 20B:732-735, 1974.

Smith, L.; Sandquist, G.; Olsen, D.; Arnett, G.; Gentry, S. and Kolff, W.J. Power Requirements for the AEC Artificial Heart. Trans. Amer. Soc. Artif. Int. Organs, 21:540-544, 1975.

Sandquist, G.M.; Smith, L. and Olsen, D. Plutonium-238 as a Power Source for Medical Application. Abst. Amer. Soc. Artif. Int. Organs, Vol. 4, 1975.

Smith, L.; Sandquist, G. and Kolff, W.J. Power Requirements for the AEC Artificial Heart. Abst. Amer. Soc. Artif. Int. Organs, Vol. 4, 1975.

Sandquist, G.M.; Smith, L. and Kolff, W.J. Plutonium-238 as a Heat Source for the Artificial Heart. Proc. 10th Intersoc. Energy Conversion Eng. Conf., pp. 18-22, 1975.

Smith, L.; Olsen, D.; Sandquist, G. and Kolff, W.J. A Totally Implantable Mechanical Heart. Europ. Soc. Art. Organs, November, 1975.

Smith, L.; Sandquist, G.; Olsen, D. and Kolff, W.J. Twenty-One Day In Vivo Evaluation of the ERDA Totally Implantable Mechanical Heart. Abst. Amer. Soc. Artif. Int. Organs, Vol. 5:75, 1976.

Sandquist, G.M.; Smith, L.; Olsen, D. and Kolff, W.J. Visual Studies of the Flow Field in a Mechanically Driven Blood Pump Ventricle. Abst. Amer. Soc. Artif. Int. Organs, Vol. 5:70, 1976.

Kolff, J.; Sandquist, G.; Smith, L. and Olsen, D. The Nuclear Heart. Res. Staff Phys., pp. 83, 1976.

Sandquist, G.M.; Smith, L.; Olsen, D. and Kolff, W.J. Visual Study of the Flow Field in the Mechanically Driven Artificial Heart Blood Pump Ventricle. Trans. Ann. Conf. Eng. Med. Biol., pp. 392, 1976.

Appendix 1 (Continued)

Smith, L.; Olsen, D.; Sandquist, G. and Kolff, W.J. Ventricular Balance of the Nuclear Powered Artificial Heart. Abst. Amer. Soc. Artif. Int. Organs, Vol. 6:81, 1977.

Smith, L.; Olsen, D.; Sandquist, G.; Nielsen, M. and Kolff, W.J. An Electrically Powered Artificial Heart. Trans. Ann. Conf. Eng. Med. Biol., 1977.

Sandquist, G.M.; Smith, L.M.; Bifano, N.; Romine, J. and Kolff, W.J. The Development and In Vivo Evaluation of an Integrated Electrically Powered Mechanical Blood Pump. Proc. Intersoc. Energy Convers. Eng. Conf., pp. 1050-1053, 1978.

Jarvik, R.L.; Smith, L.M.; Lawson, J.H.; Sandquist, G.M.; Fukumasu, H.; Olsen, D.B.; Iwaya, F. and Kolff, W.J. Comparison of Pneumatic and Electrically Powered Total Artificial Hearts In Vivo. Trans. ASAIO, pp. 593-599, 1978.

Sandquist, G.M.; An Analytical Model for Circulatory System Behavior. Abst. Int'l. Soc. Artif. Int. Organs, Vol. 3(A):40, April 1979.

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