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BIOLOGICAL EFFECTS OF IMPLANTED NUCLEAR
ENERGY SOURCES FOR ARTIFICIAL HEART DEVICES

Progress Report

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ABSTRACT

This work involves a study of the biological effects of radiation from mock plutonium power sources in dogs and a study of the feasibility of a tissue heat sink for waste heat from such sources in calves. It is also designed to evaluate effects of heat and radiation from plutonium sources in calves. The work is part of a program to evaluate the use of plutonium as a power source for an artificial heart device. A total of 60 dogs have been implanted with mock plutonium sources (producing a similar radiation flux as plutonium but having no associated heat) at levels of from 1 to 70 times the expected radiation flux from a 30 watt plutonium source. Results up to 4.5 years after implantation indicate that mammals may be able to tolerate the radiation flux from such sources. Results in calves indicate that 30 watts of additional endogenous heat can be dissipated to a connective tissue covered heat exchanger with a surface area of 494 cm^2 providing a heat flux of 0.06 watts/cm^2 .

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I. INTRODUCTION AND SCOPE

During the past seven years, this organization has been under contract with the Division of Biomedical and Environmental Research of ERDA to evaluate aspects related to the development of an artificial heart device. At the present time we are evaluating two areas of this development program. The first of these investigations is designed to evaluate the biological effects of gamma and neutron radiation from 30 watt ^{238}Pu power sources which will be used as a power source in an artificial heart system. This involves a long term study of 62 Labrador retriever dogs which have been implanted with simulated ^{238}Pu power sources in an attempt to determine what biological effects may result from long term neutron and gamma radiation at this level. The second area being investigated is related to the ability of the body to adapt to the additional endogenous heat from a 30 watt ^{238}Pu heat source as well as a determination of any possible synergism of heat and radiation on the elaboration of biological effects from plutonium power sources.

The first part of this report deals with the biological effects of mock plutonium power sources in dogs, while the second section is concerned with the dissipation of additional endogenous heat, these studies being performed in calves.

II. Biological Effects of Radiation from Mock ^{238}Pu Power Sources in Dogs

A. Experimental Protocol

In order to provide a radiation flux similar to that of

^{238}Pu without any associated heat, a mock source, consisting of ^{252}Cf to provide the neutron flux and part of the photon flux plus ^{90}Sr - ^{90}Y Bremsstrahlung to provide the additional required photon flux was devised. This combination was shown to provide a total neutron and photon flux and total radiation exposure similar to that of ^{238}Pu . These sources were placed in a spherical stainless steel implantation capsule and implanted in the left flank of adult labrador retriever dogs. (Fig. 1)

Five groups of 12 dogs each were implanted between 1969 and 1973. Four source configurations were employed. A source that produced the same radiation flux as a 30 watt ^{238}Pu source was designated a 1X source. Configurations delivering 5, 15, or 70 times the flux of a 30 watt ^{238}Pu source were designated 5X, 15X, and 70X. The first group contained four animals with blank capsules, four with capsules containing 15X sources, and four containing 70X sources. An additional four groups were implanted and each of these contained 4 blanks, 4 - 1X and 4 - 5X sources. Also, two animals which were the offspring of one of the 70X bitches (#254) and were irradiated continually during gestation and lactation have been included in the clinical study.

The projected kill date was variable for the first group, and ranged initially from 1 to 5 years for the other groups. Because of a lack of clinical response seen in the 1X and 5X animals, however, the kill dates for these animals was extended to from 2-10 years (Table 1).

For all animals used in the study, a battery of clinical tests has been performed at monthly intervals. Each animal has had a series of 5 determinations of each of the profile parameters performed before implantation. Monthly evaluations of this same profile have also been made for each animal after implantation for comparison with that individual's preimplantation data and with the population mean. Therefore each animal, to some extent, acts as his own control. The studies include evaluation of hematological parameters, serum electrolyte determinations, liver function evaluations, kidney function analysis, etc. (Table 2). Periodic sperm counts of all dogs in the study have also been determined.

The radiation dose rate to various organs and surfaces resulting from the implantation of a 70X source is given (Table 3). Equivalent doses for the smaller sources and total accumulated dose over time for any of the source configurations can be determined by suitable calculation.

When killed at either the end of the pre-determined observation time or as a result of degeneration of the preparation, a complete post-mortem examination of all animals has been made.

B. Results

1. Summary to date

Of the total of 60 animals implanted, 38 are still alive. Nine of the animals in the first group were killed at intervals of from 3.5 months to 2.5 years after implantation; animals were destroyed when the preparation had degenerated to the point of sloughing (usually due to latent infection at the implant site). Additionally,

two of the blanks in this group were killed for comparison purposes. Thus, three of these animals are alive, this includes one 15X animal and 2 blanks. The first group containing blanks, 1X, and 5X animals was killed in 1972 and constituted the 2 year study group. The results from this group were discussed in detail in a previous progress report. Also, during the past year animal #612, implanted on 1/29/71 died unexpectedly. This animal will be discussed in detail later. Thus a total of forty dogs are still alive. This includes 38 implanted animals and the two offspring of dog #224.

2. Clinical findings

Very little clinical change has been noted as a result of chronic irradiation of these animals. A summary of selected clinical data results as a function of time is shown (Table 4). It can be noted that with increasing time, the total white count and lymphocyte count decreased, particularly in the 15X and 70X animals. This effect is much less notable in the 5X animals and virtually non-existent in blanks and 1X animals.

With regard to sperm counts, complete or almost complete cessation of sperm production occurred within 3 months to one year of implantation in the 15X and 70X animals. The changes are much less pronounced in the 1X and 5X animals (Table 5). While no significant differences can be noted between blank, 1X, and 5X animals at any individual sampling date, if the data are pooled, there is a significant reduction in sperm count of the 5X animals when compared to blanks, while there is no significant difference between 1X and

blank animals. This decrease in sperm count corresponds nicely with the lesions seen in the testes as reported in previous progress reports.

3. Post Mortem Findings

(a) Implantation site

Pathologic changes noted at the implantation site appeared to be more severe with increasing radiation dose (Table 6). Thus, while all of the blanks, 1X, and 5X animals killed appeared to have thin viable connective tissue capsules surrounding the implants, 15X and 70X animals demonstrated more severe reactions ranging from pyogranulomas to pyogranulomas with tumor production. Tumors occurred in two 70X animals and are felt to be possibly radiation related since they occurred at unusual sites for the type of tumor seen. Demonstrations of the lesions seen at the implant site were provided in last year's progress report (C00-3167-103).

(b) Other Post-Mortem Lesions

Pathologic findings other than those at the implantation site are summarized in Table 7. Significant lesions were seen only in the lymphoid, hemopoietic and genital organs and these lesions showed a high degree of correlation with the clinical findings of blood cell counts and sperm counts.

C. Bitch #612

On 1/29/71 this bitch, a mature black Labrador retriever was implanted with a 5X source and was designated as a member of the 10 year group to be killed on 1/29/81. The clinical data on this animal revealed no abnormalities and its weight in September of 1974

was 48 lbs. Around the beginning of November of 2974 the bitch was noted to be losing weight. Weight loss continued and by the first of December it was noted that the animal was vomiting approximately one to one and one-half hours after eating a dry expanded ration which was the standard diet for all animals in the study. The appetite remained good but the vomition persisted. If a canned ration mixed with milk was fed, the animal did not vomit. However, weight loss continued despite dietary therapy.

At about this time an enlarged right popliteal lymph node was noted as well as a small (1 cm diameter) mass associated with the mammary glands. An aspiration biopsy of the popliteal lymph node was non-diagnostic being reported as fibrous tissue.

The animal continued to lose weight and died on 12/29/74. The autopsy reports on this animal are enclosed as Appendix I. Essentially, a large tumorous mass was found just distal to the stomach involving the anterior duodenum (Fig. 2). Extensive metastases were noted to many other organs including the liver, lungs, and one rib (Fig. 3). Microscopic sections of the main lesion in the duodenum and lung metastases are shown (Figs. 4 & 5). The diagnosis, based on histologic findings was a neurogenic sarcoma of the duodenum, i.e. a malignant nervous tissue tumor of the intestine.

Calculated radiation dosages to various organs of this animal are shown (Table 8). It can be assumed that the duodenal area received approximately the same radiation dose as the spleen (about 1150 Rad) over the four year period of implantation.

While this tumor type is relatively rare in dogs, it cannot be stated that this is a radiation induced tumor. Interestingly, however, this is the third animal in this study which has developed a tumor. Two animals in the 70X group developed tumors at the implantation site; one tumor was a mast cell sarcoma, and the other a fibrosarcoma (see previous progress reports). Therefore three mesenchymal tumors have occurred in this group of sixty dogs for a tumor incidence of 5%. Also, these tumors have occurred in relatively young animals (all less than six years of age) whereas tumors are generally seen more frequently in older animals.

In summary, the results of our studies to date indicate that mammals may well be able to tolerate the chronic, low level radiation from 30 watt plutonium sources since no clinical abnormalities have been noted in 1X animals implanted for periods up to four and one-half years and no significant pathological changes have been seen in 1X animals implanted for up to two years. Definite changes have been seen in animals receiving higher radiation dosages (5X, 15X, and 70X) with the severity of the changes corresponding to increasing dose rate and total dose. These changes have ranged from decreased lymphocyte counts and sperm counts seen on clinical evaluations to degenerative lesions seen at the implantation site and depletion of proliferative elements in lymphoid and hematopoietic tissue. The occurrence of tumors in three of this group of sixty dogs raises the possibility of an effect of long term low level radiation on tumor induction and, therefore, continuation of the evaluation of these animals for periods of time up to ten years is planned.

III. Implantation of 30 watt ^{238}Pu Sources in Calves

Our studies with mock plutonium sources have indicated that man may be able to withstand the radiation from 30 watt ^{238}Pu sources. Also, studies at other research institutions have shown, using blood tube heat exchangers, that pigs can withstand the additional endogenous heat from 30-50 watt heat sources. It seemed rational therefore to begin studies of the combined effects of heat and radiation from plutonium sources in the same animal.

Also, because of possible problems with blood tube heat exchangers, it was felt that an investigation of the possibility of using a tissue interface heat exchanger was indicated. The rationale and approach is detailed in the proposal for this report dated July 3, 1974 and essentially involves the gradual adaptation of the connective tissue capsule of a heat exchanger to increasing levels of heat through the use of an external cooling circuit to remove lesser amounts of heat with increasing time after implantation. During the past year investigations have been initiated to evaluate the feasibility of a tissue interface heat exchanger and to begin long term studies of the effects of heat and radiation from 30 watt ^{238}Pu sources.

The specifics of the experimental approach will be detailed below. Essentially it involved fabrication of a heat exchanger similar in size and weight to the thermal converter unit being developed by Westinghouse Astronuclear Laboratory as the Intermediate Thermal Converter Unit for the ERDA artificial heart device. This

heat exchanger was made water tight and fitted with fluid inflow and outflow tubes which could be brought through a silastic percutaneous tube and connected to a fluid pump with its associated temperature control and monitoring equipment situated outside the experimental animal.

The heat exchanger device was covered with dacron velour and implanted retroperitoneally in the right flank of 200 lb. male Holstein-Friesian calves. Two experiments were performed. In the first the heat exchanger was implanted without the plutonium source. Thereafter water at increasing temperature was circulated through the heat exchanger until the animal was dissipating 30 watts or greater through the surface of the exchanger to the connective tissue surrounding the implant.

In the second experiment, which is still in progress, the plutonium source was installed in the heat exchanger before implantation. In this case the temperature of the inflow water was gradually increased until the inflow temperature exceeded outflow temperature to the extent that, including heat loss in the tubing, the full heat load from the source was being dissipated across the heat exchanger surface. While this experiment is still in progress, the calf has been dissipating 29 watts for a period of more than 4 weeks at the time of preparation of this report.

METHODOLOGY

Experiment I - Calf MS-1 - Hot water calf

1. Mock Thermal Converter

The objective in designing and fabricating the implantation device used in the two experiments conducted to date and reported herein was to simulate approximately the size, weight, volume and outside configuration of the Westinghouse Intermediate Thermal Converter (Table 9a). Internally the device had to hold a 29 watt ^{238}Pu heat source and provide for cooling initially through a cooling fluid pumped in from outside the animal and ultimately through the walls and covering of the implanted device.

The mock thermal converter constructed was a water filled stainless steel envelope with the heat source held approximately in the center. Water, used as a coolant and a media for transfer of heat from the source to the outer shell of the device, was circulated from outside the body. This design was adequate for the experiments for which it has been employed, namely to assess whether an animal could adapt and dissipate up to 30 watts of power directly to the connective tissue surrounding the implant. Design considerations for long term implantation studies are to be discussed later in this report.

Implant Fabrication

The mock thermal converter used in these experiments is shown in figures 6, 7, and 8. Basically it was constructed from three stainless steel beakers plus fabricated stainless steel components.

The base of the device consists of two 600 ml Volbrath stainless steel beakers, the top lip cut off one and the base of the other

welded to the first to form a closed cylinder. A hole was cut in one side of the base assembly and a conical flange welded over the opening. To this flange a threaded collar was attached. The top of the mock converter, i.e. the region where the heat source would be located in the actual converter, was fabricated from a 125 ml beaker and fitted with a threaded adapter so that it could be screwed onto the rest of the device. An "O" ring formed a seal between the two parts. In this way access to the inside of the device was provided.

A holder for the ^{238}Pu heat source consisted of two cylindrical cups held by rods; one from the bottom and the other fastened to a removable disk, held in place inside the threaded collar by the cap assembly. This upper support disk was perforated with three $\frac{1}{2}$ " holes and three $\frac{5}{16}$ " holes to allow coolant passage between the base and cap of the device.

Cooling was provided through two stainless steel tubes (OD .065", wall .009") which passed through a hole in one end of the base. These tubes were held to a disk by brass pressure fittings; the disk being held over the opening in the end of the base by 6 machine screws and sealed with an "O" ring. The inflow tube opened at the side of the heat source so that flow is initially tangent to the source and then tended to circulate around the source. The opening of the inflow was crimped down to an inside diameter of about .040" to further increase turbulence inside the implant. The outflow tube was enlarged to $\frac{1}{8}$ " OD inside the device to reduce

back pressure (a modification not shown in figure 9b). In order to insure circulation in the top of the implant and to insure that no more than a small bubble of air could be trapped in the device the outflow tube was directed through the upper disk of the source holding assembly and opened with a beveled cut actually in contact with the uppermost portion of the cap on the side of the implant which was to be closest to the midline of the calf. In this manner the outflow was collecting from the highest point whether the calf was standing or lying on either side.

Outside the main envelope of the mock converter two .065" tubes were bent in an arc so that they ended in a direction parallel to the vertical axis of the device. This was done so that in the position in which the device was to be implanted the cooling tubes could run up the inside of the skin of the flank of the calf and egress high enough on its side so as not to be in contact with the animal's stall either while standing or lying down. Silastic tubing (a) (.104" x .192") was expanded slightly by soaking in xylene and slipped over the full length of the stainless steel tubes up to the holding disc. After allowing for shrinkage, the silastic tubes were clamped to the metal tubing with stainless steel suture wire and further sealed with "Silastic" Medical Silicone Adhesive (b). To protect the curved metal tubes outside the body of the device, a 1/2" stainless steel tube bent to the same radius arc was slipped over the silastic covered .065" tubes and fastened with a flange, "O" ring and machine screws to the end of the device. Both this protective tube and the small silastic tubes

(a) Dow Corning Corp., Midland, Mich.

(b) Type A; Dow Corning Corp., Midland, Mich.

which course to the outside of the animal were encased in a 5/16" x 1/2" Medical Grade "Silastic" tube. Again expansion with xylene aided in this fabrication.

Implant Covering

The entire mock converter was coated with dacron velour (c) cemented to the metal with Silastic adhesive. The adhesive was first applied to a modest area of the device. In an effort to distribute a uniform layer a serrated or "saw tooth" straight edge was used to spread the adhesive (thread gauge indicating tool; 9 threads per inch). Precut and prefitted patches of dacron velour were then applied to the freshly applied adhesive and gently pressed into the adhesive by rubbing lightly with a curved spatula.

This procedure produced a rather uniform layer of covering (silastic layer averaging about 0.7mm thick). However in some cases the ridges of silastic produced by the smoothing tool were not totally flattened when the velour was applied. In order to get a smoother and slightly thicker coating with less air entrapment the adhesive was thinned slightly with xylene in the second experiment. Here spreading of the adhesive was accomplished with a thin brass plate with a straight working surface of 2 cm in length. Three fine wires (hypodermic needle cleaning wires) were soldered at right angles to the spreading edge of the tool and cut off 0.9 mm from the spreading edge. With a little practice a smooth layer of adhesive could be applied without air entrapment or voids.

In order to facilitate ingrowth of tissue and anchoring of the cooling tubing where it emerged through the skin of the calves, a

(c) Patch #6108; US Cl. Div. of C. R. Bard, Inc. Billerica, Mass.

four inch segment of this tube was also coated with dacron velour (Fig. 8).

Sterilization of the implant and attached tubing was accomplished with ethylene oxide gas in a plastic bag inside a stainless steel container. A small hole was made in the container through which tubing was passed to carry water to cool the device during sterilization (important only when the ^{238}Pu heat source was loaded).

Heat Dissipation of Mock Thermal Converter

Two parameters were of prime interest in these experiments:

(1) power dissipated (watts) through the envelope of the mock converter and (2) the surface temperature of the device. Calculation of values for these parameters required measurement of inflow and outflow coolant temperatures, flow rate and body temperature plus a determination of the coefficient of heat transfer across the implant wall and covering.

Inflow and outflow water temperatures were measured with flexible, vinyl covered thermistor probes (d) inserted into a section of $\frac{1}{4}$ " x $\frac{3}{8}$ " flexible plastic tubing (Tygon) (e) which were connected to the silastic tubes leading into the implant. The thermistors were centered in the tubing and water directed around them by wrapping them with a "cork screw" coil of vinyl covered copper wire. Water flow tubes and leads of the thermistors were connected by use of "Y" shaped plastic tubing connectors attached 16 cm from the lead end of the probe. The heat sensitive lead end of the thermistors were positioned immediately distal to the junction with the silastic leads from the implant.

- (d) Model 401, Yellow Springs Instr. Co.; Yellow Springs, Ohio
- (e) Norton; Akron, Ohio

The thermistors were plugged into one leg of a Wheatstone Bridge circuit, fabricated in house, and the voltage imbalance due to the temperature dependent resistance of the probes was measured using a digital voltmeter(f). Calibration of the system was accomplished by measuring potential when individual probes were immersed in water, the temperature of which was changed by about 1°C temperature increments over a range of 20°C to 55°C. Sensitivity of the system was found to be 0.02°C per 0.1 mV.

Power dissipation (watts or calories per unit time) is calculable from the difference in temperature of inflow and outflow water and the flow rate. In the first experiment no heat source was loaded into the mock converter. Rather heated water was introduced through the inflow line. Thus,

$$W = (T_I - T_O) F (1/14.3) \quad (1)$$

Where W = Watts dissipated

T_I = Input water temperature (°C)

T_O = Output water temperature (°C)

F = Flow rate of water (g./min)

14.3 = Calories/min equal to 1 watt.

It is recognized that there are corrections to this equation to account for the specific heat of water at the measured temperature as well as for air content of the water. However, the errors introduced when these corrections are not made are less than the precision of other measurements going into these calculations and thus were omitted.

(f) Digitec, Model 263; United Systems Corp., Dayton, Ohio

In order to calculate the average surface temperature of the mock converter when implanted it was necessary to experimentally measure the coefficient of heat transfer across the walls of the device and through the silastic and dacron covering. This coefficient (K) represents the power dissipation (watts) per degree C difference between the inner surface and outer surface of the device:

$$K = W / (T_1 - T_2) \quad (2)$$

where,

W = Watts

T_1 = Temperature inside device

T_2 = Outer surface temperature

For each experiment K was determined by immersing the device in a highly stirred 30 gallon tub of distilled water, initially at room temperature. Water at about 40°C was pumped through the mock converter at 105 to 114 ml/min. (50°C H₂O in a second measurement of each experiment). After the temperature of the outflow water stabilized readings of inflow temperature, outflow temperature, and bath water temperature were recorded every minute for at least 15 minutes. From average readings K was calculated. Watts dissipated was calculated using equation 1; the temperature of the outflow water used as T_1 and the average bath temperature was used as T_2 . In experiment I K = 7.54; in experiment II K = 6.63 watts per degree centigrade. This difference can be attributed to differences in the thickness of the silastic covering in the two experiments.

By rearranging equation 2 and combining it with equation 1, it was possible to solve for the mean surface temperature of the mock converter when it was implanted.

For conditions of experiment 1:

$$T_2 = T_1 - W/K \text{ (from eq. 1)} \quad (3)$$

Substituting eq. 1 for W:

$$T_2 = T_1 - \frac{(T_I - T_0) \cdot F / 14.3}{K} \quad (4)$$

and since $T_1 = T_0$

$$T_2 = T_0 - \frac{(T_I - T_0) \cdot F}{14.3 K} \quad (5)$$

where T_2 = mean surface temperature of implant

T_0 , T_I , F, K defined above.

Using the same measurements plus body temperature it is also possible to assess the efficiency of energy dissipation by the tissue. By dividing the observed wattage by that expected if the implant had been placed in a water bath of body temperature (X100) one obtains a value for per cent efficiency, (%E). Using equation 1 for wattage:

$$\%E = \frac{\text{observed } W}{\text{ideal } W} \times 100 = \frac{(T_I - T_0) \cdot F / 14.3}{(T_I - T_0') \cdot F / 14.3} = \frac{T_I - T_0}{T_I - T_0'} \quad (6)$$

where T_0' = expected outflow water temperature of implant in H_2O .

If one uses equation 5, setting T_2 to body temperature and solving for T_0 it is possible to get a value for T_0' ;

$$T_0' = \frac{14.3K T_2 + T_I^F}{F + 14.3K} \quad (7)$$

and substituting in 6

$$\%E = \frac{(T_I - T_0').100}{T_I - \left(\frac{14.3K T_2 + T_I^F}{F + 14.3K} \right)} \quad (8)$$

Additional Equipment and Apparatus

The calf plus all other necessary equipment were housed in a ventilated 11' x 29' animal room with the temperature of this room maintained between 65°F and 70°F during Experiment I.

Calf Stall

A wooden "metabolism" type stall was constructed to restrain the calves during these experiments. This was a 28.5"(W) x 77"(L) x 56"(H) slat sided stall with stanchion and feed bunk adjustable to fit the length of the animal. The floor was rubber covered plywood except for a short section of steel grating which was positioned to allow urine to flow through to a collection pan. This floor was elevated from the room floor by 15 inches. An automatic water bowl was placed in the feed bunk and connected through a hose to a supply of cold water. The only unique feature of the stall was a boom arrangement which consisted of a 1"x3" wood slat held 75" above the floor of the stall at right angles to the length of the stall. This boom was positioned to be over the shoulders of the calves and extended out

past the edge of the stall on one side. The purpose of this boom was to hold a line, through the use of pulleys, which supported the cooling tubes going to the calf on one end and a counterweight on the other end.

External Heating - Cooling Loop

A schematic diagram of the external water flow system of Experiment I is shown (Fig. 10a). A peristaltic pump (g) forced 105 to 115 ml/min through a $1/3"$ x $1/2"$ silicone rubber pumping tube. The water was then forced through 25 feet of $3/16"$ x $1/4"$ copper tubing coiled in a 6 gallon water bath (h). The water in the bath was covered with a thin layer of mineral oil to reduce evaporation. From the water bath to the calf the heated water was carried through a $1/8"$ x $1/4"$ plastic tubing (Tygon) covered with $1/2"$ x $1 1/2"$ Armaflex (i) flexible pipe insulation. This tube was attached to the thermocouple assembly described above. Both input and output thermocouple assemblies as well as most of the silastic tube leading into the calf were also covered with the pipe insulation. Water leaving the calf was directed through a flow meter (j) and then into a stoppered 1 liter Erlenmeyer flask and then back to the pump. Since the water was drawn out near the bottom of the flask, the flask served as an air trap. Another tube connected this flask with a 4 liter Erlenmeyer flask containing water. This second flask was positioned 7" higher than the pump and thus served both to induce a slight positive pressure at the pump and as a water reservoir for system. An additional section of tubing was also connected with a "T" to the outflow tube between the flow meter and smaller Erlenmeyer flask. This tube was normally clamped off, but

- (g) Model 1201 Havard Apparatus, Millis, Mass.
- (h) Model 2156 American Optical, Buffalo, N.Y.
- (i) Armstrong Standard
- (j) No. 13. Roser Gilmont Instrument, Inc., Great Neck, N.Y.

when a flow measurement was to be made the clamp was removed and placed between the "T" and the flask. By measuring the amount of water expelled in a measured length of time an accurate flow rate could be determined.

Distilled water was used as the heat conducting medium. This water was boiled to remove most of the air. The system was flushed with new water weekly.

Water bath temperature was regulated by the built in control during the first portion of the experiment; however due to temperature fluctuations and difficulties in setting to desired temperature a mercury thermoregulator switch was employed during the latter part of Experiment I and throughout Experiment II. This switch was connected to a circuit which activated a relay switch through the use of a single transistor. This in-house constructed circuit controlled the power relay of the water bath.

During the first experiment when no heat source was in the implant the only danger of the animal receiving more than the intended heat load was if the water bath overheated. To safeguard against this possibility a second thermoregulator switch was placed in the water bath. This switch was connected to another relay circuit which provided power to the pump so long as the bath temperature did not exceed the safeguard limit set.

Temperature Measurements

As described earlier, the thermistors were plugged into one leg of a Wheatstone Bridge circuit and readings of imbalance of potential converted to temperature. A multiposition switch allowed

for selection of individual thermistors to be read. In practice readings were made alternately on input and output thermistors every half minute, usually for the duration of two on-off cycles of the water bath (approx. 15 min.). Average readings were used in the calculations.

In order to continuously monitor the inside temperature of the implant a recorder (k) was used to monitor the outflow thermistor circuit. In order not to load the bridge and get a large enough signal for the recorder a D. C. Vacuum tube Voltmeter (1) was used as an amplifier.

Adjustments of temperature measurements due to heat losses between the thermistors and the implant were made based upon in vitro tests. For losses outside the calf a dummy loop of tubing of the same length, diameter, encasing and insulation as the actual tube used was placed between the inflow and outflow connections at the thermistors. With this shunt lying on the back and side of the calf measurements of flow, water temperatures, room air temperature, etc. were made. The maximum loss was 1.5 watts and occurred when the inflow water temperature was 49°C (highest temperature reached in either experiment). All temperatures and calculations reported herein include appropriate corrections.

Heat dissipation through the tubing inside the animal, including through the tube shield of the implant, was measured by two methods and found to be between 3 and 4 per cent of that dissipated through

- (k) Model PRR, Texas Instruments, Inc., Houston, Texas
- (1) Model 412 A; Hewlett Packard, Loveland, Colorado

the body of the implant. At 30 watts this amounted to 1 watt passed through the tubing inside the calf. Since the surface area of tubing in the two calves averaged 15% of that of the total surface of both the mock converter and the attached tubing it can be seen that the surface of the tubing within the animals was considerably cooler than that of the body of the implant. Unless otherwise noted in this report all wattages reported are total values for dissipation within the calves.

Skin Temperature

In order to ascertain whether some of the added energy burden was lost locally through the skin a comparison of the surface temperatures of the skin covering the implant and of that of skin on the other side of the calf was made. A small thermistor was sandwiched between two thin 1" square copper plates. One side was insulated with asbestos and a $\frac{1}{2}$ inch layer of foam insulation. Hair was clipped from the skin to be examined and a thin layer of heat conducting silicone paste was applied to the exposed side of the copper plate. The thermistor assembly was held on a specific site for 8 minutes, a time period long enough for the thermistor readings to stabilize.

2. Implantation of MS-1 (hot water calf)

The experimental animal was a male Holstein-Friesian calf weighing approximately 240 lbs. at the time of surgery. This calf was adapted for a period of 4 days to the metabolism stall in which he would be kept after surgery. All food was restricted from the animal on the evening of 12/15/74 and surgery for implantation was accomplished on 12/16/74.

The calf was anesthetized by coning using a metaphane gas anesthesia machine. After anesthesia was accomplished, an endotracheal tube was inserted and surgical anesthesia maintained by an oxygen, metaphane mixture through the endotracheal tube.

After placing the calf in left recumbency, the right flank area was shaved and prepared for surgery using alcohol and betadine scrubs. The animal was then transported to the surgery where all materials needed were in place.

A ten centimeter skin incision was made in the mid right flank area extending dorso-ventrally from a point approximately five cm below the lumbar hypaxial musculature to a point approximately five cm above the ventral mid line. The external and internal abdominal oblique muscles were penetrated by blunt dissection and the fascia of the transversus abdominis muscle was incised. At this point an attempt was made to separate the rectus abdominus muscle and fascia from the underlying parietal peritoneum but this was found to be impossible to accomplish because of the close adhesion between the two structures. Therefore a large pocket was formed by digital probing between the rectus and the transversus muscles, this pocket being large enough to contain the heat exchanger device.

At this point the heat exchanger was removed from its sterilization covering and disconnected aseptically from the circulation pump by pinching off the inflow and outflow tubes with hemoclips, cutting (with sterile scissors) the connections, which were then discarded, and dipping the ends of the severed tubes in a sterilizing solution (betadine).

The heat exchanger was then placed in the preformed pocket after which a subcutaneous tunnel was prepared to a point on the flank approximately 5 cm anterior to the incision site and 5 cm ventral to the hypaxial musculature. After the tunnel was formed, a stab incision was made at the skin site and the silastic tube containing the inflow and outflow tubes was passed from the pocket, through the skin tunnel and out through the stab incision in the skin. It was positioned such that about half of the four inch length of dacron velour surrounding the tube was located subcutaneously under the skin and half was outside the skin surface.

At this point the heat exchanger was reconnected to the circulating pump. The total time during which the heat exchanger was disconnected from the circulating pump approximated five minutes. While this time interval was not important in this experiment, it would become very important in the next experiment in which the plutonium source would increase the outside temperature of the device while disconnected and the final temperature reached would depend upon the total disconnection time.

After placement of the device, the muscle layers, subcutaneous tissues and skin were closed routinely and the animal returned to the stall. The entire surgical procedure took less than one hour.

3. Progression after surgery

a. Heat Incrementing

Thermal data for Experiment I are listed in Appendix 3 and shown (Fig. 11).

Due to a rather slow recovery from surgical anesthesia the heating water tubes of calf I were not connected to the pumping apparatus until 8 hours after surgery. Since no nuclear heat source was used in this experiment the implant remained at body temperature during this period. For the next 16 hours water was pumped into the implant at approximately body temperature. From day 1 to day 23 the temperature of the input water was gradually raised until it reached 49°C at which time the calf was absorbing and dissipating 30 watts from the mock thermal converter. For a period of 21 days thereafter inflow temperature was held constant. The calf was then euthanized for tissue examinations. Throughout the experiment the flow rate was maintained between 105 and 115 ml/min. Previous in vitro tests had shown that below 50 ml/min. a marked stratification of temperature layers occurs but can be avoided at rates above this.

The progression of heat build-up was somewhat triphasic in this experiment. Within $2\frac{1}{2}$ days the power dissipated was up to 8 watts and then raised more slowly for a period of 10 days. The design was to introduce moderate heat levels to stimulate vascularization and yet allow for post operative healing around the implant to occur. During the third week the increases in input water temperature were more rapid. On day 18 the calf seemed to be experiencing some discomfort as exhibited by kicking itself and its stall and frequent lying and standing. At this point (25 watts having been attained) the inflow water temperature was reduced slightly. A resumption in heat incrementation did not bring forth a similar response again and 30 watts

was attained and maintained with little further discomfort exhibited by the calf. It was later found that the band around the chest of the calf was irritating the skin and was replaced by an open weave nylon mesh belt to allow for better air circulation to the skin. Thus, it is unclear if the implant was the only, or the main, source of discomfort on day 18.

As can be seen from the enclosed data the inside temperature of the implant, as measured from the outflow water temperature, reached 45.2°C to 45.4°C when 30 watts was reached. Calculated surface temperature of the device rose to 41 degrees C by day 2, but leveled off at 41.2 to 41.3°C later during the experiment. Maximum surface temperature reached was calculated to be 41.7°C . The efficiency value has been described previously but for this experiment can also be interpreted as the relative drop in temperature between the inflow water and the device surface compared to the drop between the inflow water and the average body temperature. This efficiency value rose from about 60% early in the experiment to 80% when 30 watts was achieved. Since the surface temperature of the device did not change greatly during the experiment this efficiency value is interpreted to indicate an adaptation to the heat load, probably through increased vascularization.

Body temperature in this calf was in the high normal range but tended to fall slightly during the course of the experiment even

though the burden of heat was increasing. As the wattage levels approached 30 watts during the build-up phase some perspiration was noted as indicated by a slightly moist haircoat.

There were three system failures during this experiment. This was not unexpected since one of the reasons for conducting the trial without the ^{238}Pu source was to check out shortcomings of the system. During the night of the 14th and 15th day the water bath temperature exceeded the selected cutoff temperature and the pump shut off for about 12 hours. During the night of the 31st to 32nd day there was a blockage in the inlet orifice of the implant which caused a build-up in pressure resulting in a leakage of water. As a result flow was interrupted for 12.5 hours. Early in the morning of the 43rd day a pumping tube ruptured and resulted in no flow for 5 hours. During each of these incidents the implant returned to body temperature. When heat dissipation was resumed, a drop in wattage was noted, as well as the calculated efficiency value. This depression lasted for about one day. The exact nature of changes which occurred are unknown but are probably at least in part due to vascular changes. Appropriate modifications in the system were made after each incident to minimize the chance of a reoccurrence.

The skin surface temperature at the implantation site was found to range between $.56^{\circ}\text{C}$ and $.86^{\circ}\text{C}$ higher than that of the skin at a comparable location on the other side of the calf.

Appetite and growth of the calf during the experiment were very good. Water consumption, while not measured, did not appear to be excessive.

b. Clinical Progression

Healing of the surgical site occurred uneventfully. There was no serious swelling or infection in the surgical area and the sutures were removed ten days after surgery. The skin incision where the percutaneous lead penetrated also healed completely with no untoward reaction and absolutely no infection at the penetration site.

The only clinical parameter that was measured in this animal was body temperature and this remained within normal limits during the entire time of the study.

4. Termination and Post-Mortem Evaluation

As mentioned previously, the animal was brought up to a heat dissipation of 30 watts gradually and this level of heat dissipation, representing 0.06 watts/cm^2 of surface area was attained at three weeks after surgery (Fig. 11). The animal was maintained at this level of heat dissipation for three weeks. Thus the total period of implantation was six weeks. At the end of this time period, on 1/27/75, the animal was killed and a complete post-mortem examination performed. The autopsy report is included as Appendix II.

The animal was disconnected from the circulation pump and taken to the Autopsy Room of the College for destruction. A photograph taken immediately previous to killing demonstrates the condition of the animal at this time (Fig. 12). Particularly noteworthy is the complete lack of any untoward reaction at the implantation site of in the area of the percutaneous lead.

The calf was killed with an overdose of Na- pentobarbital. Opening of the peritoneal cavity revealed a section of omentum adhered to the parietal peritoneal surface with a number of prominent blood vessels attached (Fig. 13). The heat exchanger was invested with a connective tissue covering. Over most of the surface of the device, the fibrous connective tissue capsule was intact and apparently viable. However, at one point on the cutaneous side of the neck of the implant, the dacron velour had become detached from the surface of the device, and, in this area, some necrosis of the investing connective tissue capsule was evident (Fig. 14). This area was relatively small (approx. 0.5 cm in diameter) and viable connective tissue surrounded the necrotic focus.

Other than the two findings of adhesion of the omentum to the peritoneal surface adjacent to the heat exchanger and the small necrotic focus in the connective tissue capsule surrounding the implant, no other abnormal gross post-mortem findings were observed.

Histological examination of the connective tissue capsule surrounding the device showed a mild fibrotic reaction with numerous foreign body giant cells around the hairs of the dacron velour (Fig. 15). The connective tissue capsule had an extensive blood supply; however, it could not be categorically stated that this vascular response resulted from the gradually increasing heat applied to the capsule, since this type of connective tissue is normally quite vascular.

As a check on this vascularity, another calf was implanted with a spherical stainless steel hollow ball (as used in the dog phase of

this study) which had been covered with dacron velour. This animal is still alive, and will be sacrificed at an appropriate time. The histological appearance of the connective tissue capsule from this implant, to which no heat had been applied, will then be compared to that from those devices to which heat had been applied.

5. Conclusions

The results obtained in this first experiment indicated that, by gradually increasing the heat applied to a heat exchanger of this size (494 cm²), the body of the calf can adapt and develop mechanisms sufficient to dissipate 30 watts of power through the connective tissue surrounding the device without appreciable tissue damage. This amounts to a heat dissipation of about 0.06 watts/cm². Although it took three weeks to attain a heat dissipation of 30 watts, this does not necessarily indicate that three weeks is a minimum time to accomplish this amount of heat dissipation. It is possible that by incrementing heat input at a more rapid rate, the desired level of 30 watts could be attained more rapidly. Experiments during the next year will be designed to evaluate this aspect.

This experiment does indicate, however, that the previously accepted maximum non-deleterious heat input level of 0.03 watts/cm² is probably an underestimate. It may indeed be that one could go considerably beyond the level of 0.06 watts/cm². This was not attempted since the concensus is that a 30 watt power source would be the largest needed to power an artificial heart device and that the

implantable version of the thermal converter unit would not be much smaller than the 500 cm² figure employed here.

Experiment II - Calf MS-2 - plutonium source calf

1. Introduction

The previous experiment was designed, basically, to evaluate all procedures of the implantation and handling processes using an empty heat exchanger, so that any possible problems might be noticed and corrective measures taken before the implantation using the 28.4 watt source. This experiment was completely successful and, as a result, it was possible to achieve a power dissipation of over 30 watts by circulating hot water through the heat exchanger device.

The second experiment, which is still in progress, was, therefore, very similar to the first with the exception that in this case the plutonium source was present in the heat exchanger and water circulation was used as a coolant to control the amount of tissue heat loss, rather than as a source of heat. This required some modification of the control and monitoring procedures as described below.

2. Methodology

The experimental design and apparatus of the second experiment was very similar to that of the first except in procedures and equipment concerned with using the ²³⁸Pu heat source and with efforts to overcome problems or reliability brought to light by Experiment I.

The mock thermal converter was again covered with silastic adhesive and dacron velour, and thermal conductivity measurements were made. In order to load the ^{238}Pu heat source the upper (removable) source holder of the device was placed, cup end up, on a pedestal consisting of a 1" brass rod with short cylindrical protrusions on top which fit into the openings to the upper source holder. The heat source was first cooled with room temperature distilled water and then placed on the upper source holder. The base of the mock converter was then inverted and slid down over the source until contact was made with the holder attached to the base. The whole assembly including the pedestal was then inverted, the pedestal removed and the cap screwed on. The junction of the cap and base was sealed and coated with silastic adhesive. Cooling of the mock converter was started as soon as the source was loaded and continued through the period of sterilization until the time of implantation.

The accessory equipment required to regulate the cooling of the implant while in the calf was largely the same as that of the first experiment. Only the differences are noted here. A schematic diagram of the system is enclosed (Fig. 10b).

A trap in the waterline was added between the pump and water bath. In Experiment I small slivers of rubber seemed to flake off of the inside of the pumping tube due to the action of the pump. These tended to restrict flow at the input opening inside the implant.

A secondary emergency pump was added to the system. This pumped room temperature water into the implant if one of two conditions

occurred: (1) water flow from the primary system dropped below 30 ml/min., and (2) temperature of the outflow water of the implant exceeded a preset level. One-way check valves were included in the system so that one pump could operate if a failure occurred in the other. A large reservoir of distilled water (22 gal.) served as the source for the emergency system.

In order to detect flow stoppage the ball type flowmeter used in Experiment I was encased in a wooden block with a hole passing through the block at right angles to the long axis of the flowmeter. A lightbulb was placed at one end of this hole and a light sensitive diode at the other end. A circuit was designed and constructed which activated the emergency pump if the ball in the flowmeter dropped into the path of the light beam (30 ml/min. or less).

In order to detect a high temperature in the outflow line a second thermistor was used in the outflow line near the exit from the calf. Another circuit was constructed which would also activate the emergency system if the temperature exceeded a selected (adjustable) temperature.

When the emergency circuit is activated it also turns on a 1 rpm. motor operated cam which activates a reset microswitch once each minute. If the condition triggering the emergency circuit was only temporary the emergency circuit is shut off, if not it continues to be activated until given attention. A warning system consisting of flashing lights and a buzzer detectable outside the animal room is also activated by the emergency system. Signs have been posted and personnel instructed to notify the investigators if the warning system is activated.

A pressure gauge was added to the system in order to detect the development of a blockage or partial blockage in the lines. Also the pumping tubing is changed frequently to guard against ruptures. Water is flushed weekly with samples assayed for possible radioactive contamination.

3. Implantation

The implantation procedure for this experiment was very similar to that employed previously. A 200 pound male Holstein-Friesian calf was adapted to the metabolism unit as before. It was prepared for surgery, anesthetized and surgically prepared as before. The only significant change in the surgical procedure was that, in this case, the subcutaneous tunnel was made and the percutaneous lead passed through it to the outside before the device was placed in the retroperitoneal location. This was done so that reconnection to the circulating pump could be made more rapidly and thus avoid excessive heat build-up in the device during implantation. As a further precaution, the exchanger was cooled by circulating water at about 32°C through it before disconnection for placement of the percutaneous silastic tube. Cool water was also circulated through the device during the closure procedure in order to avoid excessive heat build-up while the animal was disconnected and transported from the surgery to the stall room after surgery.

The total time of disconnection of the device from the circulating pump was less than three minutes during surgery, and less than five minutes during transport of the animal from the surgery to the stall room.

4. Heat Incrementing

Thermal data and calculated parameters are enclosed (Fig. 16 and Appendix IV).

From the time the animal came out of surgery until it was able to stand in its stall (6 hr.) water was circulated in and out of the implant into a 6 liter flask which held distilled water at a temperature about 30°C. Once the calf was hooked to the regular cooling system, the cooling temperature was raised so that the calf was immediately dissipating heat from the ^{238}Pu source. The temperature of the inflow water was raised over a period of 21 days so that the increase in wattage dissipated by the calf was nearly linear in this experiment. On day 21 the inflow water temperature exceeded the outflow temperature very slightly and thus the calf was dissipating the full power of the ^{238}Pu source (28.4 watts). The power dissipation level is being held at full power at the writing of the progress report.

It may be noted that the inside temperature seems to be dropping slightly during the 3½ week period the calf has been at full power. The calculated implant surface temperature has averaged 41.5°C since full wattage has been achieved and has not exceeded 41.9°C. Again in this experiment the efficiency value rose from about 50% early in the experiment to approximately 75% at present.

The only interruption in the normal operation of the external cooling system occurred on day 19 when the light bulb failed in the flow detection system and thus turned on the emergency cooling pump

for 40 minutes before the condition could be corrected. Since room temperature water was used for cooling during this period it was thought best to lower the regular cooling water temperature and build the wattage back to the previously attained level (25.7 watts) over the following day (see graph). To avoid another such failure the light source of the flow detection system was changed to include 2 bulbs operating at a lower voltage to prolong bulb life and to ensure that the system would still operate even if one bulb did fail.

The room temperature of the area in which the calf is housed has been higher during this experiment than during the previous experiment. Air conditioning of the building has only recently been turned on. Thus, the calf has been exposed to air temperatures up to about 84°F. In spite of the temperature the calf has not had trouble dissipating the added energy due to the implant, nor has it exhibited any marked signs of discomfort.

5. Clinical findings

As before, this animal recovered from surgery uneventfully. A serum pocket did form at the implantation site shortly after surgery, but this regressed quickly and had completely disappeared within five days of the operation. In this experiment periodic blood samples have been taken and total white and differential counts determined both before and occasionally after surgery. The results indicate no significant changes attributable to the presence of the source (Table 20). This is not unexpected since no changes in blood counts have been discovered in 1X animals in the dog study.

Again, as before, the body temperature has remained in the normal range for the duration of the study to date.

This animal was adapted to heat by gradually increasing the heat dissipation from an original 0.01 watts/cm² to the final level of 0.06 watts/cm² over a period of three weeks as was done previously. It is desirable to keep this animal alive at the 0.06 watt per cm² level for as long as possible. However, it will probably be necessary to terminate the experiment within a few weeks due to the growth of the calf and the restricting length of the implanted cooling tubing even if no system failure occurs. Unfortunately, it is impossible to disconnect the animal from the circulating pump because of the layering effect of the heated water in the exchanger which will result in the top of the device developing an interior temperature approximately 6°C hotter than the bottom if circulation is discontinued. If this was allowed to occur the power dissipation per unit surface of the implant would have to nearly double on the upper half of the device. It is hoped that modification of the heat exchanger will allow prevention of this layering effect and thus permit complete separation of the circulating pump in the next experiment.

IV. Conclusions

The data gathered during these two experiments indicates that the body of the calf can adapt to the dissipation of at least 0.06 watts/cm² across the surface of a heat exchanger device to the investing connective tissue capsule if the heat build-up is allowed

to occur gradually. This, therefore, allows the consideration of dissipation of all waste heat from the thermal converter unit to the connective tissue capsule surrounding it rather than diverting this waste heat to the blood pump as previously proposed. Thus, this approach provides another option for waste heat disposal if the blood pump mechanism for heat removal should prove undesirable or unworkable.

TABLE 1

Groups and Status of Dogs in Biological Effects of
Cardiac Nuclear Power Source Study

<u>Group No.</u>	<u>Implant Year</u>	<u>No. of Dogs</u>	<u>Sources</u>	<u>Observation Time</u>	<u>Kill Year</u>	<u>Status</u>
I	1969	12	15,70 x nominal	?		9 killed, 3 alive
II	1970	12	1,5 x nominal	2 years	1972	Killed
III	1970	12	1,5 x nominal	10 years	1980	In Progress (one dead)
IV	1971	12	1,5 x nominal	7.5 years	1978	In Progress
V	1973	12	1,5 x nominal	5 years	1978	In Progress

TABLE 2

Physiological Parameters Monitored In
Labrador Retriever Colony (40 dogs)

<u>Parameter</u>	<u>Normal Value</u>	<u>S.D.</u>
Blood Studies		
Total WBC	12863	1791
Packed Cell Volume	43	3.3
Differential WBC		
Bands	0.2	0.3
Segmenters	62	5.6
Lymphocytes	25	3.7
Monocytes	7	1.1
Eosinophils	6	4.0
Serum Electrolytes		
Sodium (mg/l)	173.7	10.5
Potassium (mg/l)	7.1	0.8
Calcium (mg %)	11.0	0.6
Serum Proteins		
Total Protein (gms %)	6.4	0.6
A/G ratio	1.50	0.26
Serum Enzymes		
SGOT	42	13.5
SGPT	46	18.6
Serum Lipase	0.4	0.2
Prothrombin Time	9.8	0.8
Blood Sugar	82	9.0
Blood Urea Nitrogen	18	2.0
Serum Creatinine	0.94	0.17

TABLE 3

Dose Rates to Various Organs and Surface Sites from Source Capsule
Containing 500 mCi $^{90}\text{Sr}^*$ and 0.373 g $^{252}\text{Cf}^{**}$

<u>Site</u>	<u>Distance to Surface of Capsule (cm)</u>	<u>Dose Rate (mrads/hr)</u>
<u>Internal</u>		
Descending Colon	3	1100 $\pm$ 150
Spleen	6	460 $\pm$ 62
Liver	19	60 $\pm$ 4
Cecum	16	190 $\pm$ 13
Kidney	17	190 $\pm$ 17
<u>Surface</u>		
Left flank (over capsule)	0.5	1600 $\pm$ 100
Anterior testes	15	88 $\pm$ 28
Eye	67	2.0 $\pm$ 2
Thyroid Gland	51	26 $\pm$ 8

* Measured in cadaver

** Estimated from PNL studies

Table 4

SUMMARY OF CLINICAL DATA

BLANKS

TIME (mos.)		WBC ($\times 10^{-3}$)	LYM (%)	PCV (%)	SGPT (SF units)	TP (gms %)	BUN (mg %)	GLU (mg %)
Pre. Impl.	$\bar{x}$	14.9	24.1	43.1	28.5	6.5	18.9	80.6
	SD	4.3	7.2	4.6	14.4	.8	3.8	16.3
1-6	$\bar{x}$	13.6	22.2	44.6	30.1	6.5	18.7	77.4
	SD	4.5	7.7	6.6	16.2	1.3	4.2	21.6
7-12	$\bar{x}$	13.0	23.2	44.4	31.5	6.6	18.6	73.2
	SD	4.3	7.3	7.8	17.6	.9	5.5	17.5
13-18	$\bar{x}$	13.2	21.0	44.7	33.1	6.7	19.0	70.7
	SD	4.4	6.7	8.3	14.8	1.0	5.5	15.9
19-24	$\bar{x}$	13.6	20.8	45.2	34.5	6.6	19.9	72.4
	SD	3.3	7.0	3.5	18.3	.7	6.2	11.8
25-30	$\bar{x}$	15.8	18.1	46.4	35.3	6.5	20.0	70.5
	SD	5.9	6.2	3.4	16.5	1.0	4.9	17.5
31-36	$\bar{x}$	12.7	22.2	46.1	29.4	6.2	17.9	70.8
	SD	3.2	7.1	3.2	17.0	.8	6.2	20.4
37-42	$\bar{x}$	12.6	21.8	47.3	35.7	6.3	15.8	75.5
	SD	4.7	7.3	3.1	17.3	.8	6.4	12.5
43-48	$\bar{x}$	13.4	20.2	45.6	33.3	6.3	15.0	65.1
	SD	3.4	7.7	3.2	19.8	.7	7.1	9.0
49-54	$\bar{x}$	13.5	19.4	45.6	30.7	6.7	19.0	80.0
	SD	3.1	5.7	2.8	18.7	.6	3.9	14.3
55-60	$\bar{x}$	12.3	21.7	44.9	38.9	6.6	18.4	70.9
	SD	1.9	6.1	4.4	42.4	1.0	4.6	11.6
61-	$\bar{x}$	15.1	20.5	44.1	21.5	7.1	15.9	65.0
	SD	3.9	7.2	2.5	12.7	.4	2.5	7.1

Table 4 Continued

SUMMARY OF CLINICAL DATA

IX

TIME (mos.)		WBC ($\times 10^{-3}$)	LYM (%)	PCV (%)	SGPT (SF units)	TP (gms %)	BUN (mg %)	GLU (mg %)
Pre. Impl.	$\bar{x}$	14.5	22.8	45.1	35.2	6.66	20.0	81.8
	SD	3.8	7.4	3.5	16.5	.97	4.3	22.2
1-6	$\bar{x}$	13.8	20.5	43.8	27.5	6.24	20.1	75.3
	SD	5.0	6.7	7.8	14.9	.91	4.3	20.7
7-12	$\bar{x}$	12.4	22.1	46.0	32.3	6.73	21.5	72.4
	SD	3.3	7.4	6.9	16.5	1.21	5.2	17.4
13-18	$\bar{x}$	13.3	18.6	45.1	37.7	6.64	20.2	68.9
	SD	4.8	7.8	8.8	15.4	1.34	5.2	13.1
19-24	$\bar{x}$	14.0	16.9	45.9	34.0	6.61	20.3	74.0
	SD	4.1	6.7	3.4	16.6	.75	5.0	15.9
25-30	$\bar{x}$	14.9	17.0	45.4	38.7	6.22	21.0	77.7
	SD	4.1	6.1	6.4	16.2	1.16	5.5	13.9
31-36	$\bar{x}$	12.6	20.2	46.6	26.2	5.88	17.9	81.2
	SD	4.1	7.9	4.4	13.1	.68	4.2	16.2
37-42	$\bar{x}$	11.9	20.6	47.0	37.2	6.10	18.1	79.9
	SD	2.9	6.2	2.9	16.2	.94	4.0	14.3
43-48	$\bar{x}$	11.2	23.8	46.3	28.3	6.40	18.2	73.9
	SD	2.6	9.0	3.1	19.3	.85	3.1	10.6
49-	$\bar{x}$	13.6	22.8	42.2	21.1	6.82	19.7	71.8
	SD	5.3	8.2	4.4	13.5	.53	3.4	11.1

Table 4 Continued

SUMMARY OF CLINICAL DATA

		<u>5X</u>						
TIME (mos.)		WBC ($\times 10^{-3}$)	LYM (%)	PCV (%)	SGPT (SF units)	TP (gms %)	BUN (mg %)	GLU (mg %)
Pre. Impl.	$\bar{x}$	15.0	22.8	44.7	32.9	6.5	19.1	85.7
	SD	6.3	6.3	3.5	18.8	.8	4.3	20.4
1-6	$\bar{x}$	13.3	22.7	45.7	28.3	6.3	19.7	73.5
	SD	4.2	7.4	3.9	13.7	1.0	4.2	20.7
7-12	$\bar{x}$	12.3	21.9	46.4	32.3	6.5	21.1	70.1
	SD	3.8	6.1	4.0	14.8	1.4	5.8	14.7
13-18	$\bar{x}$	11.7	18.9	46.4	35.3	6.5	20.8	71.6
	SD	2.9	7.8	3.9	15.1	.9	5.0	16.4
19-24	$\bar{x}$	11.8	17.5	45.8	34.3	6.7	20.4	73.6
	SD	2.4	6.0	3.6	17.9	.9	4.2	10.7
25-30	$\bar{x}$	12.4	19.6	45.5	40.2	6.1	18.5	77.4
	SD	3.0	6.2	3.9	16.5	1.0	4.9	13.1
31-36	$\bar{x}$	10.4	19.3	45.5	30.7	5.6	17.2	85.2
	SD	2.3	5.9	3.7	14.4	.6	3.4	16.1
37-42	$\bar{x}$	9.9	21.0	45.1	38.9	6.0	15.6	77.5
	SD	2.6	5.4	3.9	19.8	.7	3.4	16.7
43-48	$\bar{x}$	9.3	19.5	46.5	31.2	6.6	15.4	82.2
	SD	1.9	6.2	3.0	31.2	.5	3.2	12.2
49-	$\bar{x}$	8.6	15.0	46.7	--	6.9	13.7	70.0
	SD	1.8	1.0	2.5	--	.3	1.5	0

Table 4 Continued

SUMMARY OF CLINICAL DATA

		<u>15X</u>						
TIME (mos.)		WBC ($\times 10^{-3}$)	LYM (%)	PCV (%)	SGPT (SF units)	TP (gms %)	BUN (mg %)	GLU (mg %)
BI	$\bar{x}$	11.1	24.4	43.3	59.1	6.4	17.9	76.1
	SD	3.0	6.1	2.3	17.5	.7	2.1	2.0
1-6	$\bar{x}$	11.0	19.1	45.0	45.6	6.8	15.0	78.0
	SD	3.2	7.1	2.4	21.7	1.2	3.2	16.4
7-12	$\bar{x}$	8.2	19.6	45.4	29.2	6.7	17.8	74.0
	SD	2.6	5.1	3.1	12.9	.7	4.0	18.4
13-18	$\bar{x}$	8.7	16.4	46.6	28.8	6.8	18.7	77.9
	SD	2.6	5.2	2.6	13.3	1.3	4.1	20.6
19-24	$\bar{x}$	9.1	15.4	46.1	29.6	6.4	16.1	73.0
	SD	2.3	6.2	2.4	12.3	1.3	2.7	14.4
25-30	$\bar{x}$	10.2	13.5	47.4	47.9	6.2	17.3	70.1
	SD	2.3	5.5	3.1	17.2	.6	2.7	13.2
31-36	$\bar{x}$	9.6	15.0	47.2	27.4	6.9	18.8	75.7
	SD	2.6	7.0	2.9	12.2	1.2	2.0	13.5
37-42	$\bar{x}$	13.1	13.8	46.7	40.5	6.0	18.9	81.3
	SD	3.6	6.8	3.5	11.2	.7	3.2	13.9
43-48	$\bar{x}$	12.5	12.3	48.2	30.4	5.5	18.8	66.5
	SD	2.2	4.8	3.6	5.9	.7	6.1	6.3
49-54	$\bar{x}$	12.0	13.7	50.4	34.8	6.1	17.8	81.0
	SD	6.3	6.7	4.8	10.5	.9	3.4	4.2
55-60	$\bar{x}$	9.0	12.3	47.5	39.2	5.7	18.3	79.0
	SD	2.6	7.2	2.3	23.3	.5	2.5	26.4
61-	$\bar{x}$	8.1	11.5	49.5	23.3	6.0	17.3	72.8
	SD	1.1	3.8	3.0	11.0	.5	2.6	9.5

Table 4 Continued

SUMMARY OF CLINICAL DATA

		<u>70X</u>						
TIME (mos.)		WBC ($\times 10^{-3}$)	LYM (%)	PCV (%)	SGPT (SF units)	TP (gms %)	BUN (mg %)	GLU (mg %)
BI	$\bar{x}$	13.3	21.0	44.2	-	5.4	19.8	73.7
	SD	3.0	5.0	1.2	-	0.8	1.7	5.8
0-5	$\bar{x}$	13.2	14.2	41.4	44.8	6.9	17.3	76.3
	SD	-	2.9	2.5	12.8	0.8	1.0	6.9
6-11	$\bar{x}$	7.2	10.8	39.3	29.3	7.0	14.8	85.7
	SD	8.2	4.7	0.6	18.8	0.4	0.9	7.2
12-17	$\bar{x}$	7.9	10.4	41.4	35.7	7.0	18.3	73
	SD	-	-	-	-	-	-	-
18-24	$\bar{x}$	9.4	8.5	38.5	23.9	7.0	18.6	71
	SD	-	-	-	-	-	-	-

Table 5

SPERM COUNTS OF DOGS IMPLANTED WITH
SIMULATED ^{238}Pu POWER SOURCES

IMPLANT TYPE	SPERM COUNT (PER MM^3) $\times 10^5 \pm \text{S.D.}$					
DATE	11/70	12/71	4/72	6/73	3/74	10/74
BLANK	---	4.2 ± 2.1	2.6 ± 2.1	2.4 ± 0.5	2.6 ± 1.6	2.1 ± 0.7
1x	1.3 ± 0.9	4.1 ± 0.3	2.0 ± 2.2	1.8 ± 0.8	1.8 ± 0.9	2.0 ± 1.6
5x	0.9 ± 0.6	2.8 ± 1.3	1.2 ± 1.3	1.3 ± 0.9	1.2 ± 0.8	1.5 ± 0.7
15x	0.7	---	---	---	---	---
70x	---	0	0	---	---	---
NORMAL	1.5 0.8					

Table 6

CONDITION OF IMPLANT SITE AT AUTOPSY

IMPLANT	DOGS NO.	TVC*	TVC MNI**	TVC NIL+	PG++	PG TUMOR	f DOSE (Rads)
0	6	5	1				0
1X	4		1	3			500
5X	5	2		3			2,500
15X	3	2			1		11,700
70X	4				2	2	19,000-49,000

*TVC - Thin Viable Capsule

**MNI - Mononuclear Reaction

+NIL - Necrotic Inner Layer

++PG - Pyogranuloma

Table 7

SUMMARY OF LESIONS SEEN AT AUTOPSY
(ANIMALS KILLED 3 - 47 MONTHS AFTER IMPLANT)

SYSTEMS

<u>TREATMENT AND NO.</u>	<u>CIRCULATORY</u>	<u>RESPIRATORY</u>	<u>DIGESTIVE</u>	<u>URINARY</u>	<u>GENITAL</u>
0-6	Mild Mitral Fibrosis	Focal Chronic Pneumonia	Typhlitis and Esophagitis	Pyelitis Urethritis Ascarid Granulomas	Mild Prostititis Hyperplasia of Uterine Mucosa
1X-4	Mild Mitral Fibrosis	---	Mild Lymphoid Hyperplasia	Pyelitis Ascarid Granulomas	Hyperplasia of Uterine Mucosa
5X-5	Medial Mineralization Aortic Arch Tumor Metastasis	Mild Pneumonia Tumor Metastasis	--- Neurogenic Sarcoma	Focal Nephritis	Mineralization of Prostrate Tumor Metastasis
15X-3	Endocardial Hemorrhage Aortic Mineralization	Pulmonary Edema, Fibrosis	Esophageal Hyperplasia Enteritis	Heteroplasia of Urinary Bladder Ascid Granuloma	Hypospermatogenesis
75X-4	Mild Valvular Fibrosis Mineralization Aorta	---	Ulcerative Esophagitis; Mucosal Hyperplasia	Hemorrhage of Heteroplasia; Tumor Metastasis	Prostatitis Aspermatogenesis

Table 7 Continued

SUMMARY OF LESIONS SEEN AT AUTOPSY (cont.)
 (ANIMALS KILLED 3 - 47 MONTHS AFTER IMPLANT

SYSTEMS

<u>TREATMENT AND NO.</u>	<u>ENDOCRINE</u>	<u>CNS</u>	<u>LYMPHOIC</u>	<u>HEMOPOEITIC</u>	<u>SKELETAL</u>
0-6	---	---	---	---	---
1X-4	---	---	---	---	---
5X-5	---	---	Tonsillar Hyperplasia, Tonsillitis Tumor Metastasis	---	Hip Dysplasia, Osteoarthritis Tumor Metastasis
15X-3	---	---	Lymphoid Atrophy	Myeloid Hyperplasia	Hip Dysplasia Osteoarthritis
70X-4	---	---	Lymphoid Atrophy, Splenic Hemopoiesis	Bone Marrow Hypoplasia	Hip Dysplasia Osteoarthritis

TABLE 8
RADIATION DOSAGE TO VARIOUS ORGANS OF BITCH #612

<u>ORGAN</u>	<u>DISTANCE</u> (cm.)	<u>DOSE RATE</u> (m Rads/hr)	<u>TOTAL DOSE</u> (Rads)
Decending colon	3	80.21	2752.81
Spleen	6	33.57	1152.12
Liver	19	4.29	147.23
(L) iliac plexus	5	42.29	1451.39
(R) iliac plexus	15	16.07	551.52
Cecum	16	13.96	479.11
Kidney	17	13.96	479.11

Table 9

PHYSICAL CHARACTERISTICS OF WESTINGHOUSE ASTRONUCLEAR LABORATORY
INTERMEDIATE THERMAL CONVERTER AND CORNELL MOCK CONVERTER

<u>CHARACTERISTIC</u>	<u>WANL Intermediate Thermal Converter</u>	<u>Cornell Mock Converter "A"</u>
Envelope Dimensions - cm		
Height	17	17.1
Width	8.5	8.6
Length	9.5	9.8
Weight - grams		
With Pu source	1764	1597
With Al mock		1320
w/o source (H ₂ O only)		1240
Volume - cc		
w/o coupling	740	786
Surface Area - cm ²		
w/o coupling		509
Heated surface		494

TABLE 10
BLOOD CELL COUNT
FOR ^{238}Pu IMPLANT CALF

<u>DATE</u>	<u>PCV(%)</u>	<u>WBCX 10^3</u>	<u>% BANDS</u>	<u>% SEGMENTERS</u>	<u>% LYMPHOCYTES</u>	<u>% MONOCYTES</u>	<u>% EOSINOPHILS</u>
4/8/75	28	6.1	3	30	53	14	0
4/14/75	29	6.0	0	38	50	8	4
5/13/75	29	8.6	0	16	76	4	4
5/29/75	33	7.8	0	23	65	7	5

Figure 1

Radiograph of Labrador Retriever with implanted mock ^{238}Pu power source.

Figure 2

Tumor mass surrounding the anterior duodenum in bitch #612

Figure 3

Metastatic lesion in rib of bitch #612.

Figure 4

Microscopic section of neurogenic sarcoma of the duodenum in bitch #612

H & E x350

Figure 5

Microscopic section of metastasis of neurogenic sarcoma in lung of
bitch #612

H & E x110

Figure 6

Components of disassembled mock Westinghouse Intermediate Thermal Converter heat exchanger.

Figure 7

Assembled mock Westinghouse Intermediate Thermal Converter heat
exchanger.

Figure 8

Dacron velour coated mock Westinghouse Intermediate Thermal Converter Heat Exchanger ready for sterilization and implantation.

Figure 9a

Schematic Diagram of Westinghouse Intermediate Thermal Converter unit.

Figure 9b

Schematic Diagram of mock Westinghouse Intermediate Thermal Converter
heat exchanger.

Figure 10a: Experiment I: Flow diagram of coolant and controls

Figure 10b: Experiment II: Flow diagram of coolant and controls

Figure 11: Experiment I: Temperature of inflow water, implant interior, implant surface, animal body; power dissipation, and heat dissipation efficiency

Figure 12

Calf MS-1 after disconnection from circulating pump 6 weeks after implantation and 3 weeks after attainment of heat dissipation of 30 watts.

Figure 13

Abdominal cavity of calf MS-1 showing adhesion of omentum to parietal peritoneal surface under heat exchanger device. Rumen is on the right and muscle covered heat exchanger on the left.

Figure 14

Area of tissue necrosis on cutaneous side of neck of implant where dacron velour had become detached from the surface of the device.

Figure 15

Histologic section of connective tissue capsule surrounding heat exchanger device MS-1 with multinucleated giant cells investing hairs of dacron velour.

H & E x275

Figure 16: Experiment II: Temperature of inflow water, implant interior, implant surface; animal body and power dissipation

MICROPSY PROTOCOL

SUBJECT: Black Labrador Retriever No. 612
Age 4 yrs. - 8 mos.

SEX: Female

STATUS: 5X; 3 yrs., 11 mos. duration.

DIED: December 29, 1974

CASE HISTORY: In early November of 1974, the subject was noted to have lost weight. Physical examination disclosed a grossly enlarged right popliteal node and questionable generalized lymphadenopathy. Coat was in poor condition but dog was alert and without evident pain. Dog had been vomiting and was placed on high protein diet.

December 18 dog was admitted to Small Animal Clinic. Pariureal x-ray study was done of gastrointestinal system - no overt blockage was observed. Enlarged node and bone marrow were biopsied. Fibroblasts and polymorphonuclear cells indicated possible fibroma (fibrosarcoma) or granuloma. Bone marrow did not indicate neoplasia. Pronounced heart murmur was discovered during examination.

December 19 dog was returned to its cage and given 3cc combiotic daily until its death.

EXTERNAL EXAMINATION:

Subject is emaciated. Right popliteal node is enlarged. There is a c ½ inch discrete mass present in the mammary tissue of the left side just beneath the skin. Implant incision is well healed. Integument and external aspect of the implant site are not remarkable.

INTERNAL EXAMINATION:

PRIMARY INCISION - Subcutis and serous cavities are not remarkable. Lumen of the gall site is smooth with a few areas of yellowish pigment. Capsule itself is quite thin and uniform. There is a trace of liquid in the cavity but little if any evidence of inflammatory reaction in the site.

CIRCULATORY SYSTEM - Great vessels are not remarkable. A nodule was present near A-V valve of heart.

RESPIRATORY SYSTEM - Lungs contain several yellowish nodules, most prominent of which lies near the bronchus of the left lung. Sinuses and trachea are not remarkable.

DIGESTIVE SYSTEM - Esophagus is not remarkable. Stomach, and upper abdomen are involved with a large white nodular tumor mass extending down the lymphatics to the nodule in the mammary tissue on the left side. No Peyer's patches are visible in the small intestine. Rectum contains several red foci. Liver is extensively sclerotic with nodular lesions and large white plaques on the surface all lobes are involved. Except as noted above intestines are not remarkable. Pancreas was surrounded by tumor mass but not apparently involved.

LYMPHATIC SYSTEM - Thymus is involuted. Spleen is not remarkable. Nodes in head and neck are not remarkable. Both popliteal nodes are enlarged and the entire lymphatic system of the abdomen and chest appear abnormal; much has been invaded by the tumor.

URINARY SYSTEM - Kidneys, ureters, and bladder are not remarkable.

CENTRAL SYSTEM - Ovaries, especially the left, and uterus are involved in the tumor mass.

ENDOCRINE SYSTEM - Thyroids, adrenals, and pituitary are not remarkable.

CENTRAL NERVOUS SYSTEM - Not remarkable.

MUSCULOSKELETAL SYSTEM - There is an enlargement on fifth rib of the right side approximately one half inch above the costo-chondral junction. Skeletal muscle was atrophied.

Dec. 30 Dec., 1974

Case No. (K36912)

16

Owner: Kallfelz
Address: Phys. Biology

Case No.
Animal ID: 612
Veterinarian: Kallfelz
Pathologist: King

Species: Canine Breed: Lab. Ret.
Diseased? Method of Death:

Sex: F Age: 5½ yrs. Wt: 20+
Time of Death: Time of Autopsy:

CLINICAL DIAGNOSIS: Neoplasia

HISTORY: Implanted with 5x50 watt rock 238 Pu source for 4½ yrs. Has lost weight for last 6 weeks. Pats but vomits 1-1½ hrs. after.

GROSS FINDINGS: Animal in quite cachectic, anemic and slightly icteric. Small 1 cm x ½ cm present in left mid mammary gland area. Many large and small firm nodules scattered in mesovarium going up to the ovaries and down the spermatic cord remnant. Nodules also along falciform ligament to the liver with large masses in the liver proper and causing peripheral sclerosis to the masses. Large (5 cm) mass adjacent to pancreas consisting of many smaller nodules or scattered generally throughout mesenterics. Similar masses scattered in lung (approx. 50) and one in ant. ventral mediastinal area. Several pale plaque-like masses in right upper diaphragm proper and in right ventral diaphragm also. On large area of pale, firm tumor mass in myocardial septum as seen only from right heart. Several siderotic plaques on spleen. Kidneys are normal grossly as are adrenals, brain, bladder & G.I. tract proper. Large firm 8 cm mass in right popliteal space similar to vessels elsewhere. Larger masses have tiny lumen cystic spaces and yellowish-brown, mottled areas in them. Small ones are mostly pale white to grey.

GROSS DIAGNOSIS: Malignant Neoplasia - Type undetermined

MICRO: 1. Lung: Tumor cells, spindle-shaped mainly.
2. Lung: " " " " "
Liver: " " " " "

Masson's trichrome: Tumor cells are brown as is reg. smooth muscle cells.

FINAL DIAGNOSIS: Leiomyosarcoma

APPENDIX II

NECROPSY PROTOCOL

SUBJECT: Holstein calf Number MS1-4
AGE: 5 Months
SEX: Male
STATUS: Water heated capsule, 6 weeks duration
KILLED: January 29, 1975

EXTERNAL EXAMINATION

Subject is alert and in good health. Implant incisions are well healed. There is a 1 cm mass evident in flank beneath implant site; otherwise external aspect is not remarkable.

INTERNAL EXAMINATION:

PRIMARY INCISIONS - Subcutis is not remarkable. Dacron velour covering implant device is well invested with fibrous tissue and has adhered to device except for a region on the cutaneous side of the implant neck where covering has become detached. At this site there is a focus of brown-discoloration of the fibrous capsule. On the visceral side of the device the capsule has formed several adhesions to the omentum.

Percutaneous tube covering is well invested with fibrous tissue and is not remarkable.

CIRCULATORY SYSTEM - not remarkable.

RESPIRATORY SYSTEM - not remarkable.

DIGESTIVE SYSTEM - not remarkable except for omental adhesions heretofore noted.

LYMPHATIC SYSTEM - Thymus is present. Spleen and nodes are not remarkable.

URINARY SYSTEM - not remarkable

GENITAL SYSTEM - not remarkable

ENDOCRINE SYSTEM - not remarkable

CENTRAL NERVOUS SYSTEM - not remarkable

MUSCULOSKELETAL SYSTEM - not remarkable

APPENDIX III
THERMAL DATA FROM EXPERIMENT I

Day	Time	Water Flow (ml/min)	Water Input (°C)	Water Output (°C)	Implant Surface (°C)	Rectal Temp. (°C)	Power Diss. (watts)	Effi- ciency (%)
0	1900	110.0	38.90					
0	2200	110.0	38.90			39.8		
1	630	110.0	39.30			39.6		
1	900	110.0	40.70			39.7		
1	1100	110.0	40.90			39.7		
1	2100	110.0	42.30			39.7		
2	810	110.0	42.00			39.4		
2	1430	110.0	43.20			39.4		
2	1705	111.0	43.22	42.13	41.0	39.6	8.4	60.0
3	800	109.0	43.18	42.03	40.9	39.5	8.7	62.8
3	1400	108.0	42.96	41.85	40.7	39.5	8.4	64.4
3	2330	106.0	43.26	42.11	41.0	39.3	8.5	57.5
4	1130	107.0	43.20	42.04	40.9	39.2	8.6	57.8
4	2130	112.0	43.50	42.28	41.0	39.4	9.5	60.2
5	910	112.0	43.42	42.24	41.0	39.3	9.2	57.8
5	2030	110.0	43.44	42.20	41.0	39.4	9.5	61.5
6	830	111.0	43.94	42.43	40.9	39.1	11.7	63.2
6	1700	108.0	43.74	42.33	40.9	39.2	10.6	62.2
7	815	107.0	43.78	42.39	41.0	39.4	10.3	63.6
7	1500	109.0	43.80	42.32	40.8	39.1	11.2	63.2
8	800	109.0	43.73	42.17	40.6	38.8	11.8	63.8
8	2000	107.0	43.77	42.22	40.7	39.3	11.5	68.5
9	610	108.0	43.81	42.36	40.9	39.3	10.9	64.5
9	1830	109.0	43.79	42.24	40.7	39.1	11.8	66.3
10	905	107.0	43.83	42.33	40.9	39.4	11.2	67.0
10	1838	106.0	43.80	42.23	40.7	39.1	11.6	66.1
11	800	107.0	43.87	42.32	40.8	39.2	11.5	65.4
11	1325	108.0	44.29	42.55	40.8	39.3	13.1	69.2
11	1715	108.0	44.92	43.09	41.3	39.1	13.8	62.2
12	830	106.0	44.92	42.99	41.1	39.3	14.2	68.3
12	2030	105.0	45.18	43.15	41.2	38.9	14.8	63.5
13	900	103.0	44.93	42.88	40.9	39.1	14.7	68.7
13	1930	106.0	44.90	42.98	41.1	39.2	14.2	66.8
14	810	107.0	44.98	42.95	41.0	39.4	15.1	72.1
14	1645	107.0	45.76	43.52	41.3	39.5	16.7	71.1
15	930	111.0	45.67	43.44	41.1	39.4	17.3	72.1
15	1330	110.0	45.79	43.39	41.0	39.3	18.4	74.2
15	1505	110.0	46.52	43.96	41.4	39.3	19.7	71.5
16	1155	110.0	46.55	43.87	41.2	39.2	20.5	73.1
16	1920	111.0	46.68	43.94	41.1	39.1	21.2	73.3
17	743	109.3	46.44	43.87	41.3	39.4	19.7	74.0
17	1100	109.0	47.24	44.24	41.2	39.2	22.8	74.7
17	2235	110.0	47.55	44.55	41.5	39.5	23.0	75.2
18	815	108.5	47.50	44.49	41.5	39.6	22.8	76.2
18	1317	111.0	47.56	44.31	41.0	39.1	25.2	77.5
18	2243	111.0	47.57	44.39	41.1	39.3	24.6	77.7
19	815	110.0	46.56	43.82	41.0	39.4	21.0	77.7
19	2030	109.0	47.15	44.15	41.1	39.4	22.9	78.3
20	835	108.0	47.14	44.21	41.3	39.5	22.0	76.3
20	1930	108.0	47.56	44.37	41.2	39.5	24.0	79.0
21	800	108.0	47.51	44.31	41.1	39.3	24.1	78.1

APPENDIX III (Cont.)

Day	Time	Water Flow (ml/min)	Water Input (°C)	Water Output (°C)	Implant Surface (°C)	Rectal Temp. (°C)	Power Diss. (watts)	Effi- ciency (%)
21	1620	112.0	48.06	44.65	41.1	39.4	26.6	80.6
21	2145	114.0	48.25	44.84	41.2	39.3	27.1	78.6
22	823	113.0	48.24	44.72	41.0	39.4	27.7	81.3
22	2145	112.0	48.80	45.04	41.1	39.6	29.4	82.9
23	815	112.0	48.77	45.05	41.2	39.4	29.1	81.3
23	1330	112.0	49.18	45.21	41.1	39.2	31.0	81.2
23	2135	110.5	49.13	45.11	41.0	39.1	31.0	80.6
24	820	108.5	48.89	44.97	41.0	39.3	29.7	82.3
24	1135	111.5	49.13	45.05	40.8	39.0	31.8	81.9
24	1640	111.0	48.89	45.01	41.0	39.0	30.1	79.5
25	840	109.5	48.88	45.02	41.1	39.0	29.5	78.6
25	1415	114.0	48.86	45.00	40.9	39.2	30.7	81.9
26	842	114.0	48.86	45.09	41.1	39.1	30.0	79.0
26	1815	112.0	49.01	45.21	41.3	39.2	29.7	78.6
27	810	111.0	48.89	45.10	41.2	39.0	29.4	77.7
27	1945	111.5	49.03	45.21	41.3	39.3	29.8	79.7
28	821	111.5	49.13	45.13	41.0	38.9	31.1	79.3
28	1635	112.0	49.10	45.13	41.0	39.1	31.0	80.9
29	830	111.5	49.07	45.15	41.1	39.1	30.5	80.0
29	1641	112.0	49.14	45.27	41.3	39.3	30.3	79.9
30	833	110.0	49.11	45.17	41.2	39.4	30.3	81.9
30	1602	111.5	49.32	45.33	41.2	39.4	31.1	81.6
31	830	110.0	48.70	44.86	41.0	38.8	29.4	78.4
31	1630	112.0	49.11	45.28	41.3	39.3	30.0	79.8
32	1410	113.0	48.94	45.21	41.3	38.8	29.5	75.6
32	2125	112.0	49.19	45.53	41.7	39.3	28.6	75.6
33	822	112.0	49.18	45.37	41.4	38.9	29.8	75.8
33	1645	111.0	49.17	45.37	41.5	39.5	29.4	79.6
34	835	112.5	49.18	45.23	41.1	39.2	31.0	80.5
34	1900	112.0	49.21	45.24	41.1	39.2	31.1	81.1
35	835	113.0	49.17	45.28	41.2	38.7	30.6	75.7
35	1920	114.0	49.17	45.31	41.2	39.2	30.7	79.7
36	815	116.0	49.08	45.32	41.3	39.2	30.4	78.7
36	1545	114.0	49.12	45.26	41.2	39.3	30.7	80.6
37	835	115.0	49.11	45.20	41.0	39.3	31.4	82.6
37	1605	115.0	49.17	45.33	41.3	38.8	30.8	76.6
38	755	114.5	49.17	45.29	41.2	39.6	31.0	83.1
38	1640	114.0	49.21	45.29	41.2	38.8	31.2	77.3
39	809	114.0	49.17	45.25	41.1	39.7	31.2	84.8
39	1525	115.0	49.19	45.33	41.2	39.5	31.0	82.3
40	839	111.0	49.21	45.24	41.2	39.2	30.8	80.7
41	840	110.0	49.12	45.13	41.1	39.1	30.6	80.4
41	1625	115.0	49.24	45.35	41.2	39.1	31.2	79.3
42	845	112.0	49.21	45.23	41.1	39.1	31.2	80.4
42	1635	111.5	49.24	45.24	41.1	39.3	31.1	81.5
43	1325	113.0	49.15	45.34	41.3	39.2	30.1	78.2
43	2030	111.0	49.18	45.46	41.7	39.2	28.8	75.2
43	2200	111.0	49.12	45.22	41.2	39.1	30.2	79.0
44	752	110.0	49.06	45.20	41.3	39.1	29.7	77.9
44	1112	110.0	49.24	45.21	41.1	38.9	31.0	78.7

APPENDIX IV
THERMAL DATA FROM EXPERIMENT II

Day	Time	Water Flow (ml/min)	Water Input (°C)	Water Output (°C)	Implant* Surface (°C)	Rectal Temp. (°C)	Power* Diss. (watts)	Effi- ciency* (%)
0	2030	106.0	36.68	40.25	40.0	39.5	2.0	56.0
1	1150	106.0	37.77	41.04	40.4	39.2	4.2	50.8
2	816	105.0	37.72	40.98	40.3	38.9	4.6	48.3
3	821	105.0	38.29	41.37	40.5	38.7	5.7	47.9
4	2100	105.0	38.40	41.45	40.5	39.2	6.1	56.9
5	799	105.0	38.74	41.46	40.2	38.7	8.5	61.8
5	2040	105.0	38.95	41.77	40.6	38.9	7.8	56.5
6	823	105.0	39.32	41.96	40.6	38.8	9.1	59.7
6	1699	106.0	39.32	42.10	40.9	38.9	7.9	52.7
7	809	105.0	39.64	42.29	40.9	38.9	9.0	55.7
7	1603	109.0	40.14	42.59	41.1	39.2	9.8	59.2
8	631	110.5	40.56	42.87	41.3	38.9	10.6	55.5
8	1541	110.0	40.76	42.93	41.2	38.9	11.7	59.7
9	641	110.0	41.02	43.22	41.5	39.3	11.6	60.3
9	1440	110.0	41.43	43.53	41.7	39.2	12.3	58.1
10	710	111.5	41.31	43.18	41.1	38.9	13.8	63.7
10	1418	111.0	41.38	43.32	41.3	39.3	13.4	65.0
11	725	111.0	41.73	43.43	41.1	38.7	15.2	63.2
11	1735	111.0	42.09	43.92	41.8	39.4	14.2	63.1
12	804	111.0	42.15	43.62	41.1	38.8	17.1	68.4
12	1944	109.0	42.45	43.96	41.4	39.1	16.9	67.0
13	708	109.5	42.60	44.11	41.6	39.2	16.9	66.9
13	1634	108.5	42.88	44.25	41.5	39.4	18.1	70.6
14	701	109.5	43.08	44.19	41.2	38.9	19.9	71.0
14	1625	108.5	43.44	44.63	41.7	39.5	19.4	71.4
15	648	110.0	43.49	44.45	41.3	38.9	21.0	71.2
15	1620	109.0	43.88	44.77	41.5	39.4	21.7	75.0
16	710	110.0	43.97	44.65	41.2	38.9	23.2	74.3
16	1642	107.0	44.19	44.91	41.4	39.4	23.0	76.2
17	710	106.5	44.32	44.90	41.3	38.9	24.1	74.4
17	1601	103.0	44.54	45.15	41.5	39.6	24.0	78.4
18	1015	105.0	44.71	45.09	41.2	39.1	25.6	77.6
18	2045	103.0	45.08	45.47	41.6	39.4	25.7	77.2
19	826	103.0	42.87	43.87	40.7	39.1	21.2	79.1
19	931	103.0	43.35	44.40	41.3	39.1	20.9	73.5
19	1051	103.0	43.62	44.56	41.3	39.1	21.7	74.3
19	1207	103.0	44.11	44.83	41.3	39.1	23.3	75.3
19	1620	103.0	44.64	45.18	41.5	38.9	24.6	73.8
19	1944	103.0	44.90	45.32	41.5	39.3	25.4	77.4
20	646	104.0	44.92	45.33	41.5	39.1	25.5	75.2
20	1651	102.0	45.48	45.68	41.5	39.2	27.4	77.8
21	619	104.0	45.38	45.46	41.3	39.1	27.9	78.5
21	1699	104.0	45.84	45.89	41.7	39.4	28.1	78.2
22	744	105.0	45.80	45.68	41.3	38.9	29.2	77.9
22	1745	104.0	45.83	45.94	41.8	39.4	27.6	77.0
23	650	106.0	45.87	45.84	41.5	39.1	28.7	77.3
23	1704	105.0	46.00	46.07	41.9	39.7	27.9	79.0
24	655	105.0	45.96	45.89	41.5	39.0	29.0	76.8
24	1610	108.0	46.05	46.08	41.8	39.6	28.2	78.1
25	1000	112.0	46.05	45.99	41.6	39.1	28.9	75.9
25	2000	112.0	46.21	46.15	41.8	38.9	28.9	73.5

APPENDIX IV (Cont.)

Day	Time	Water Flow (ml/min)	Water Input (°C)	Water Output (°C)	Implant* Surface Temp. (°C)	Rectal Temp. (°C)	Power* Diss. (watts)	Efficiency* (%)
26	830	112.0	46.05	45.97	41.6	38.2	29.0	70.5
26	2050	112.0	46.13	46.13	41.8	39.4	28.4	76.8
27	640	112.0	46.03	46.01	41.7	38.9	28.6	73.9
27	1630	112.0	46.13	46.17	41.9	39.3	28.1	75.2
28	655	112.0	46.07	46.04	41.7	39.1	28.7	75.0
28	1635	106.0	46.10	46.12	41.9	39.1	28.3	74.3
29	655	112.0	46.06	46.05	41.8	38.6	28.5	71.3
29	1620	104.0	46.24	46.19	41.8	38.7	28.0	72.4
30	1710	102.0	46.30	46.10	41.6	38.9	29.8	76.5
32	730	103.0	46.04	45.98	41.6	38.3	28.9	71.4
33	745	104.0	46.07	45.92	41.5	38.5	29.6	74.3
34	650	109.0	46.16	46.01	41.6	38.8	29.6	75.0
35	630	109.0	46.12	45.95	41.5	38.6	29.7	74.5
36	640	109.0	46.34	46.13	41.6	38.7	30.0	74.3
37	640	108.0	46.18	45.97	41.5	38.6	30.0	75.0
38	650	107.0	46.09	45.95	41.5	38.6	29.4	74.3
40	1925	106.5	45.87	45.68	41.2	38.7	29.9	77.2
42	650	108.0	45.94	45.83	41.4	38.8	29.2	75.9
43	700	108.0	45.84	45.51	40.9	38.5	30.9	78.8
43	1430	108.0	45.82	45.71	41.3	38.6	29.2	75.5
44	631	109.0	45.67	45.62	41.3	38.6	28.8	75.3
44	1352	109.0	45.64	45.56	41.2	38.8	29.0	77.3
45	812	109.0	45.83	45.59	41.0	38.7	30.2	78.2

* The following equations were used to calculate wattage level, surface temperature and heat dissipation efficiency in experiment II:

$$\text{watts dissipated} = 28.41 + (T_I - T_O) F/14.3 \quad (1a)$$

$$\text{implant surface temperature} = T_O - \frac{28.41 + (T_I - T_O) F/14.3}{K} \quad (5a)$$

$$\% \text{ Efficiency} = \frac{28.41 + (T_I - T_O) F/14.3}{28.41 + \left(T_I - \frac{T_2 K + 28.41 + F/14.3}{K + F/14.3} \right) F/14.3} \times 100 \quad (8a)$$

where,

T_I = Input water temperature

T_O = Output water temperature

F = Flow rate

K = 6.63