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By

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On January 19, 1975, research and development programs of the U.S. Atomic Energy Commission (AEC) became part of the newly formed Energy Research and Development Administration (ERDA). In this report, since it refers to work done in 1974, most references are to AEC programs.

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• NUCLEAR POWERED PROSTHESES

The totally implantable artificial heart will dissipate waste heat. We have implanted $^{238}\text{Pu}^{16}\text{O}_2$ heat sources in the thorax (50-watt) and abdomen (29-watt) of miniature swine, one of the latter being temporarily cooled by an external percutaneous coolant loop to control surface temperatures during the tissue ingrowth period. We have designed, fabricated and implanted large discoid and smaller right parallelopiped (flat plate) devices for the study of tissue heat conductance and tolerance at various surface heat flux levels. It appears that device-tissue interface temperatures of 108°F and fluxes of at least 30 mW/cm^2 are tolerable once tissue ingrowth has occurred. At least one month following implantation is required for this state to be reached.

Biological Effects of Intracorporeal Radioisotope Heat Sources

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The objectives of this project are: 1) to study the long-term effects of heat and radiation from radioisotope heat sources typical of those intended for use in completely implantable cardiac assist and replacement systems, 2) determine the surface temperature (or heat flux) limits for tissue-ingrown devices, and 3) work in collaboration with other AEC artificial heart program contractors as required to further program progress. We have abandoned the concept of intrathoracic (intraaortic) heat source implants, having studied one such preparation and its surgical control, and devoted the past year to: a) developing suitable devices which will contain 29-watt $^{238}\text{Pu}^{16}\text{O}_2$ heat sources and can be implanted in the abdomen of miniature swine for indefinite

periods, and b) defining surface temperature limits for such devices which will permit intimate and permanent tissue ingrowth for long-term fixation and acceptance.

Thoracic Implants. In our last annual report we described the findings on animal #4442, in which an intrathoracic (intraaortic) 50-watt heat source had been in place for about 42 weeks. Occlusion and burnup resulted. Animal #4444, a surgical control having an identical implant (minus the heat source), was sacrificed approximately the same period after implantation and the findings were unremarkable. Total thrombus occlusion of the device had occurred, and the implant was surrounded by a scar tissue capsule 1 cm thick at its thickest, considerably less thick and vascular than the capsule found surrounding the hot implant in #4442. Work on such preparations was then discontinued in favor of concentrating on abdominally located sources.

Abdominal Discoid Implants. In our previous annual report we described a swine preparation in which a discoid (8 in. diameter, 3 in. center thickness, 810 cm² surface area) having a central electrical heater was implanted retroperitoneally and, three weeks later, the heater surgically replaced with a 29-watt ²³⁸Pu¹⁶O₂ heat source. Surface temperature just before surgery, with 30 watts electrical power input, was 108°F. Telemetric measurements immediately following surgical insertion of the heat source was 112°F; this dropped to a low of 110°F in 4 days, then rose to a maximum of 116°F over the subsequent 30-day period. The animal was then sacrificed. Wherever tissue ingrowth had not taken place (over the source cavity cap and around nonveloured thermistor lead sites), the tissue was grossly necrotic. The device was enveloped by a 2-cm thick scar capsule comprised of dense, grossly healthy tissue. Histologically, the basal layer (0.5 mm) of tissue immediately against the device was necrotic, however viable granulation and fibrous tissue were found in the velour nap and beyond. It is possible that 108°F is a tolerable interface temperature, and in this case it is likely that postoperative hyperthermia caused the surface temperature to rise to a point sufficient to cause surface tissue necrosis, decreasing effective heat conductance and producing the surface temperature rise subsequently recorded.

Postoperative hyperthermia, local or generalized, is common and is an important factor in implant heat tolerance. We have commonly observed temporary hyperthermic excursions following surgery or simply anesthesia in our swine (Figure 4.1), and we have no satisfactory explanation for this. It seems to be less likely if we avoid using a physiological saline drip during surgery, though injections of this same solution in rats produced no hyperthermia. Postoperative treatment with an antipyretic (Pyrilgin, a brand of dipyrone) had no detectable effect. Since device surface temperature is directly related to inflowing blood temperature, it is important to somehow control body temperature of hot device recipients throughout the period during which tissue ingrowth is taking place; in any event, the fact that periodic py-

rexia may occur in any recipient may place a practical upper limit on device surface heat flux to something below that observed in euthermic individuals.

The importance of intimate ingrowth of viable tissue at the surface of a hot implant was dramatically, if accidentally, displayed by another discoid implant experiment in which the discoid consisted of fiberglass with a flat plate heater in the center of one side. Plate heater power was adjusted automatically to produce a surface temperature of 106°F. As shown in Figure 4.2, effective tissue heat conductance rose postoperatively (as measured by the amount of power required to produce a 106°F surface temperature) until about the fourth week, when a downward trend began. At necropsy, we found that the fabric had come loose from the discoid (and plate) surface and the intervening space had filled with purulent exudate. It can be safely concluded that the downward trend in tissue heat conductance (Figure 4.2) signalled the separation of tissue-ingrown fabric and the heater surface.

A discoid implant was fabricated containing a 29-watt ²³⁸Pu¹⁶O₂ heat source and internal cooling coils. This was implanted between layers of abdominal musculature in a miniature swine (#4397) with percutaneous tubing carrying coolant (water) tubes and electrical leads to thermistors inside the implant to record surface temperature. A feedback network (Figure 4.3) monitors surface temperature and automatically turns on water to the cooling coils whenever this temperature exceeds a preset level. Contralateral retroperitoneal temperature is continuously monitored by a telemetric implant. The surface temperature was maintained at 104°F for three weeks postoperatively, then increased to 106°F. This animal continues on experiment at this time without external evidence of implant site abnormality. The presumption is that eventually the coolant will be unnecessary and all percutaneous tubes can be severed below skin level and the animal released for long-term (years) study of this abdominally-located heat source. It is hoped that in time the animal's tissues will maintain the device surface temperature

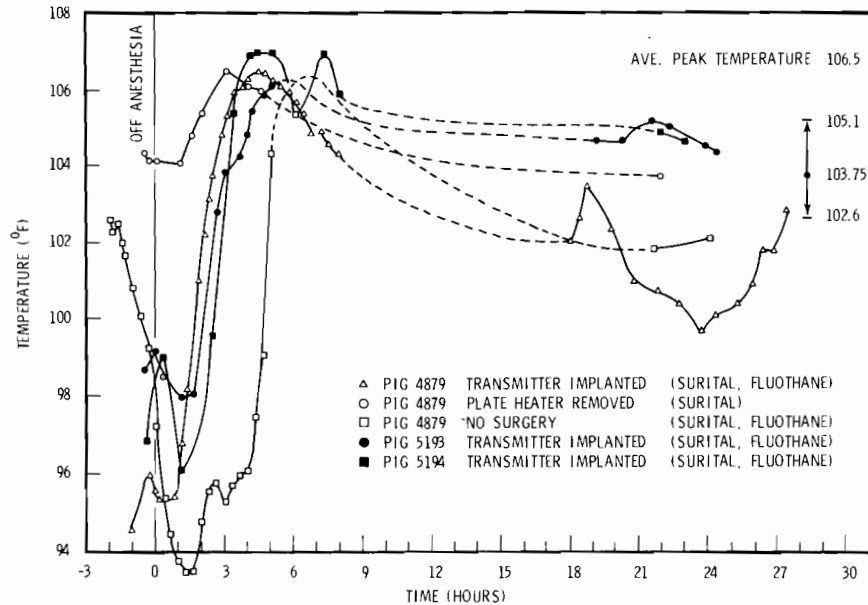


FIGURE 4.1. Hyperthermic Excursions Following Anesthesia in Miniature Swine. All temperatures were measured telemetrically from the retroperitoneal space. The anesthetics used are indicated in parentheses; in one case no surgery at all was performed. No explanation for this phenomenon has been found, though it appears to be related to the use of IV physiological saline drip during anesthesia (see text).

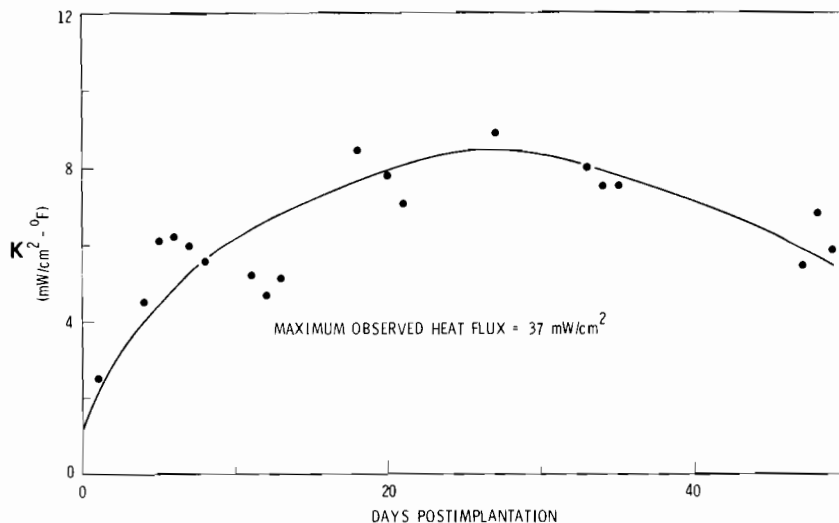


FIGURE 4.2. Variation of Effective Heat Conductance K with Time Following Retroperitoneal Implantation of a Fiberglass Discoid Containing a Flat Electrical Plate Heater on the Muscle Side. The upward trend indicates tissue ingrowth; the downward trend beginning at about 4 weeks signals separation of the velour covering from the heater surface and subsequent abscessation. Plate heater power was automatically regulated to produce a tissue interface temperature of 106°F .

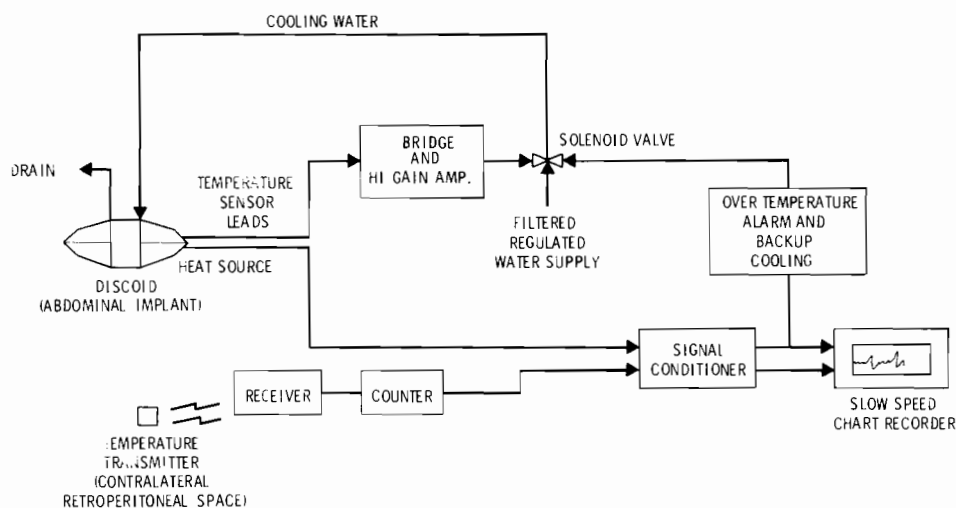


FIGURE 4.3. A Schematic Diagram of the Control System Used to Provide Water Coolant to a Radioisotope Heat Source in a Retroperitoneal Discoid Implant, Maintaining the Surface-Tissue Interface Temperature at a Preset Value.

at something less than 108°F , our best guess to date as to a maximum tolerable interface temperature.

This last preparation should prove whether the current device design is sufficient for long-term implantation of 29-watt heat sources, the primary objective of this program.

Flat Plate Heaters. Flat plate electrical heaters (Figure 4.4) were fabricated so that applied heat is dissipated from one side; the heat dissipation surface is a flat square 2×2 in., and the entire device is covered with nylon velour fabric. One was implanted retroperitoneally with the hot surface facing laterally against overlying muscle (animal #4879), and a second was implanted similarly but with the hot plate facing the peritoneum (animal #5193). Effective heat conductivity $K = \dot{Q}(T_s - T_b)$ was monitored and recorded, where \dot{Q} is the surface heat flux in watts/cm^2 , T_s is the temperature of the surface-tissue interface, and T_b is the temperature of the contralateral retroperitoneal space. The latter was measured telemetrically and is assumed to represent the temperature of blood flowing into the area of the heater implants.

In animal #4879, K ranged from 4.5 to $9.7 \text{ mW/cm}^2\text{-}^{\circ}\text{F}$, and in animal #5193

K ranged from 9.7 to $19.0 \text{ mW/cm}^2\text{-}^{\circ}\text{F}$, suggesting that the peritoneal direction affords better heat conductance during the early periods following implantation. These values should be compared with immediate postoperative K values of $1\text{-}2 \text{ mW/cm}^2\text{-}^{\circ}\text{F}$, increasing to about $9 \text{ mW/cm}^2\text{-}^{\circ}\text{F}$ in four weeks, in the case of the large fiberglass discoid having a plate heater in one surface (facing musculature), as shown in Figure 4.2. This supports two hypotheses: 1) that large implants result in lower initial effective heat conductance than small implants, 2) but with time and tissue ingrowth the differences become insignificant.

Large day-to-day differences in K are observed in addition to long-term trends upward. These variations are almost certainly due to variations in $(T_s - T_b)$, which enters into the calculation of K in a critical way when $(T_s - T_b)$ is small. Although increases in T_b will produce increases in T_s for a fixed surface heat flux \dot{Q} , the relationship is apparently not a simple one and "scatter" in K values during any experiment is the rule. Future experiments with flat plate heaters having automatically controlled surface interface temperatures are planned in an effort to define the maximum tolerable interface temperature and heat flux for retroperitoneal or abdominal intermuscular implants.

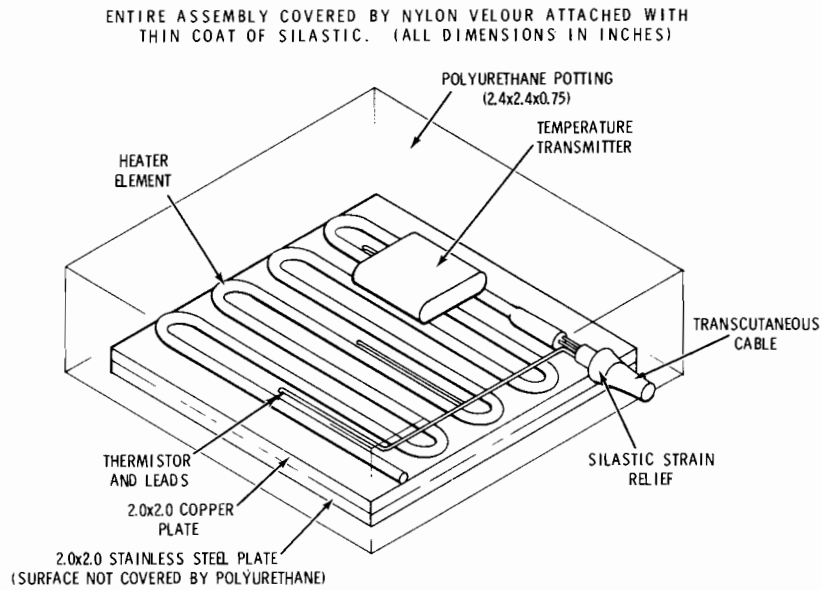


FIGURE 4.4. An Illustration of a Flat Electrical Plate Heater and Temperature Sensors (Located in the Surface Plate) Used to Study Variations in Retroperitoneal Tissue Heat Conductance with Time (and Tissue Ingrowth) and to Define Maximum Tolerable Interface Temperatures for Permanent Ingrowth of Healthy Fibrous Tissue.