

Analysis of Temperature Increase at the Device/Tissue Interface for Implantable Medical Devices Dissipating Endogenous Heat

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ABSTRACT

Active Implantable Medical Devices (AIMDs) generate heat as a result of resistive losses in their circuitry, exothermic reaction in their batteries, eddy-current heating due to inductive recharge, friction between mechanical components, etc. The European Standard which regulates AIMDs limits the heating of the outer surface of an AIMD to 2°C above normal body temperature. Despite the rapid growth in the use of AIMDs, the relationship between AIMD endogenous heat generation and tissue temperature has not been quantified. We aimed at determining the limit of endogenous heat that can be dissipated *in-vivo* by the surface area of an AIMD to remain compliant with the 2°C temperature increase limit. Four Sinclair mini-pigs underwent implantation of AIMD simulants instrumented to dissipate heat and measure temperature internally, as well as the device/tissue interface temperature. This paper presents a formula for estimating the amount of power required to raise the temperature of an AIMD based on its mechanical parameters and allowable temperature increase.

I. INTRODUCTION

The use of Active Implantable Medical Devices (AIMDs) is undergoing a rapid growth for an ever increasing number of medical indications. The majority of these are implantable pulse generators for cardiac rhythm management such as pacemakers and implantable defibrillators (approximately 1.5 million implants per year in 2006). Other implantable devices such as spinal cord stimulators, cochlear prostheses, deep-brain stimulators, nerve stimulators, drug pumps, etc. are also gaining wide acceptance, which will result in an explosive growth in the number of AIMD implants over the next few years. It is surprising thus that, in spite of the popularity of AIMDs, there is little published information available to the designer to estimate the power dissipation limits for an implantable device.

AIMDs release heat as a result of their operation. This includes heat generated by resistive losses in circuitry, exothermic reactions in batteries, friction between mechanical components (e.g. in implantable cardiac-assist pumps), etc. European Standard EN 45502-1*, which details the safety requirements for AIMDs [1], limits the heating of an AIMD under clause 17.1 by requiring that no outer surface of an implantable part of the AIMD shall be greater than 2°C above the normal surrounding body temperature of 37°C when implanted, in normal operation, or in any single-fault condition.

So far, the 2°C temperature increase limit has resulted in few, if any, design constraints for the most popular AIMDs. This is because cardiac pacemakers and neurostimulators dissipate only microwatts of power which result in negligible device temperature elevation. However, the use

* Currently, ISO Technical Committee 150, SC 6 is working to bring an AIMD standard into line with the generally acknowledged state-of-the-art and to maintain a high degree of alignment with EN 45502-1.

of devices that dissipate much more power is becoming widespread. Implantable defibrillators can deliver multiple shocks with up to 30J per pulse, resulting in significant power dissipation, for which a device-specific change to the standard allows a 2 to 4°C increase for not more than 30 minutes for these devices [2]. More recently, AIMDs are being developed with rechargeable batteries that can be replenished through transcutaneous energy transfer. These are heavily constrained by the 2°C temperature increase limit because of eddy-current heating of the device's metallic enclosure and energy losses in the battery charging process. The 2°C limit also imposes severe constraints to the design of AIMDs that incorporate pumps which commonly require a continuous power input between 5W for small ventricular assist devices and up to 25W for modern total artificial hearts [3].

The harmful effects of overheating tissue, as well as the strict regulatory requirements make it imperative to ensure compliance with the 2°C temperature increase limit. This paper describes a set of animal experiments performed to acquire steady-state *in-vivo* heat dissipation. These data are used to develop a simple, but scalable, formula for estimating the temperature increase at the outer surface of an AIMD as a function of endogenous heat levels.

II. MATERIALS AND METHODS

A. Instrumented Active Implantable Medical Device Simulants and Data Acquisition System

Five AIMD Simulants were fabricated from a deep-drawn titanium shell that is commonly used as a can for implantable pulse generators (Figure 1). The shell, manufactured by Heraeus

Medical Components, has an approximate external surface area of 74 cm² and encloses a 34 cm³ volume. The inside of the simulants consisted of a block of aluminum (ASTM: B221, 6061-T6511) machined to allow four 5Ω aluminum jacketed resistors (Huntington Electric, Inc, TMC-5, 5Ω, 1%) to be spaced evenly through the can. The outer shell of the resistors was machined to remove the protective coating and mounting flanges. Heat conductive paste (ITW Chemtronics, CT40-5) was applied between the aluminum block and resistor housings. Two type-K thermocouples were placed inside holes of the aluminum block, one approximately at the lower middle of the can and one at the upper middle of the can. The thermocouples and resistors in the aluminum block were slid inside the titanium can. Epoxy (Loctite EE0079 resin/HD0070 hardener) was poured into the can to give good thermal contact between the titanium can wall and the aluminum block/resistor assembly. The intent was that these simulants would be functionally isothermal during testing. Three more type-K thermocouples were added to the outside of the can. Two were placed touching the outer surface on each flat side of the can. The third was intended to be at least 2 cm into the surrounding tissue. The five thermocouples and wires for electrical power to the resistors (to generate heat) were routed through a large silicone rubber tube (9.5 mm outside diameter). This silicone rubber was adhered to the titanium can with medical-grade silicone rubber adhesive (NuSil Med 1511) that also covered the epoxy at the end of the can (3-5 mm thick). This silicone rubber tube was used to transition the thermocouple and electrical wires from the simulants under the skin to connectors outside the animal's skin.

A 5 meter cable of 8 pairs of Type K thermocouple wire (OMEGA 8KX24SPP) was used to connect the data acquisition system to the connectors outside the animal's skin. The cable was intended to give the animal mobility during data collection. The temperature data were collected

using a multimeter data acquisition system (Keithley model 2700) and a 20 channel multiplexer (Keithley model 7700) controlled by a personal computer. The temperature data was sampled rate of 0.22 samples/s (maximum sampling rate of the system) and then filtered by averaging over a 600s (10 minutes) period.

The instrumentation system was checked for system stability. Each simulant was placed in a 4 liter beaker at $\sim 37^{\circ}\text{C}$ and each thermocouple was required to maintain temperature readings within 0.1°C range for 60 minutes. Each simulant was also calibrated several degrees below and above the expected temperature to allow for precise compensation. The simulants were then packaged in a breathable pouch and sterilized with a hydrogen peroxide sterilization system.

B. Animal model

Experiments were conducted on four purpose-bred female Sinclair mini-pigs (40-60 kg, identified by their US Department of Agriculture numbers: USDA #6817, #6647, #6839, and #6856) that were selected as representative of typical human physiology for simulating thermal conditions related to the 2°C temperature elevation limit of implanted devices. Experiments were performed at the Skirball Center for Cardiovascular Research, Orangeburg, NY. The experiments were approved by the Institutional Animal Care and Use Committee of the Cardiovascular Research Foundation. At the end of the study, animals were necropsied to assess any potential tissue damage.

C. Simulant Implantation Procedure

For simulant implant, the animal was fasted overnight. The animal was pre-anesthetized with a mixture of Glycopyrolate 0.004-0.010 mg/kg IM, Telazol 3-5 mg/kg, and Xylazine 1-2 mg/kg. The animal was then intubated and anesthesia was maintained with isoflurane (1-3%). A pocket was made in the left abdominal wall with approximately 2 to 2 ½ cm of skin and fat over the simulant. The simulant was inserted in a knitted polyester Parsonnet™ Pulse Generator Pouch (X-Large, Bard model 002906) and tied closed. The simulant was placed in the pocket and the silicone rubber tube with the thermocouple wires and power wires was tunneled under the skin to exit the body approximately 15-20 cm higher on the abdominal wall from the simulant implant site. No data were collected at implant. All wounds were sutured closed. A bandage was wrapped around the simulant implant site to control acute edema.

D. Data collection

Data collection on each animal was started one week after implant and continued weekly for eight weeks. A data collection session started with weighing the animal and monitoring rectal temperature to check for infection. If the rectal temperature elevation was less than 0.4°C over the temperature at the time of implant, then the animal was sedated (1.5 ml Acepromazine, IM) and data collection proceeded. Data collection was started 30 minutes after the administering the sedation drug. The baseline data consisted of thermal recordings with no electrical heating of the simulant for approximately 70 minutes. Initial heating data were obtained by applying a constant voltage to the resistors inside the simulant for approximately 40 minutes. The baseline and initial heating data were then used to estimate the required power (constant voltage level setting

for resistors) for a 2°C temperature rise. A final heating data set was then obtained by driving the resistors with the calculated constant

E. Anomalies

Between data collections, the animals were able to uncover the thermocouple bandaged connectors and, throughout the 8 weeks of the experiment, pulled out some of the thermocouple wires placed outside of the titanium cans. This was despite the fact that the thermocouple wires were inside a silicone rubber tube and glued at both ends. Only in USDA #6817 were both anterior and posterior thermocouples removed, making it necessary to replace the simulant. In addition, USDA #6817 broke the sutures closing the wound causing partial exposure to the simulant by week 8.

III. RESULTS

No animal exhibited any elevated temperature that prevented data collection. Typical temperature data for week 1 are shown in Figure 3. No heat was applied to the simulant for the first 70 minutes to establish a baseline. Upon first heat application, 1W caused temperature elevation to slightly exceed the target of 2°C. Slightly less heat (0.94W) in the second application resulted in approximately 2°C elevation for the anterior and posterior thermocouples. Note that the inner thermocouples were approximately 0.5°C higher than anterior and posterior thermocouples.

Similarly, a typical temperature data plot for week 8 is presented in Figure 4. No endogenous heat was dissipated for the first 70 minutes. Upon first heat application, 0.65W caused temperature elevation to be below the target of 2°C elevation. More heat (1.45 watt) in the second application resulted in approximately 2°C elevation for the anterior and posterior thermocouples. Again, note that the inner thermocouples were approximately 1°C higher than the anterior and posterior thermocouples. This is approximately twice the difference seen acutely for the same animal (Figure 3), suggesting better heat removal by blood transport once the subcutaneous pocket heals.

After eight weeks of experimental data collection, the animals were sacrificed. The simulants and implantation sites were examined. Generally, signs of infection were observed around the entrance wound of the silicone rubber tubing. The second simulant implanted in USDA# 6817 became exposed and exhibited signs of infection. USDA #6647 exhibited signs of erosion and exposure at the silicone rubber header and along the length of the silicone rubber tube. USDA# 6839 exhibited fluid accumulation around the pocket. USDA #6856 exhibited extensive infection around the pocket and the nearby (N) thermocouple eroded through the skin. Animals were given medication during the study to control and minimize the effects of infection.

IV. ANALYSIS

Power versus temperature data points were obtained from the data by assuming the initial temperature to be an average of the last 10 minutes of baseline data (minutes 60 through 70). The temperature increase point for the initial and final heating data sets was the peak temperature

during the 40 minute recording while at a certain endogenous heating power. The composite plot for all animals is shown in Figure 5-a. The inner upper and inner lower data points for a power setting give almost identical results suggesting that the simulants were generally isothermal during data collection. From the data collected inside the titanium can, the temperature rise appears to be proportional to the power. The linear least squares curve fit for inside the can is also very consistent (correlation coefficient, $R \sim 0.98$) as shown in Figure 5-b. The thermocouples touching the outside of the can anterior (skin side) and posterior (interior side) had lower consistency for linear least squares curve fit (correlation coefficient, $R \sim 0.34$), but is still useful to provide a good estimate of *in-vivo* intersection of the least squares curve fit lines and a 2°C temperature rise as given in Table 1.

V. DISCUSSION

Data show that just outside the simulants (anterior and posterior thermocouples), the heat generated by the simulants is quite effectively transported away. This suggests that the thickness of non-perfused tissue may be approximately 1mm, as evidenced by the low temperature rise just outside the can surface. Since the radius of the surface of the can is significantly larger than the non-perfused tissue layer, the whole outer surface of the simulants can be modeled as a flat surface, and the heat flow can be approximately modeled using one dimensional heat flow equations. This is partially justified by the linear relationship of temperature versus power as exhibited in Figure 6, especially under chronic-implant conditions.

The single-dimensional approximation can be verified by comparing the estimated conduction distance to the actual can surface radius. Assuming that heat transport next to the titanium can is only through conduction and using the equation for one-dimensional heat conduction [4]:

$$q_x = \frac{Q}{A} = -k \frac{dT}{dx} \quad (1)$$

where,

$$q_x = \text{heat flux} \left[\frac{\text{J} \cdot \text{s}}{\text{cm}^2} \right], \text{ in the x direction}$$

$$Q = \text{heat flow} \left[\frac{\text{J}}{\text{s}} \right]$$

$$A = \text{normal area through which the heat is transferred} [\text{cm}^2]$$

$$k = \text{thermal conductivity of biological tissue, } 1.1 \times 10^{-3} \frac{\text{cal}}{\text{cm} \cdot \text{s} \cdot ^\circ\text{C}} = 0.0046 \frac{\text{W}}{\text{cm} \cdot ^\circ\text{C}}$$

$$dT = \text{differential of temperature} [^\circ\text{C}]$$

$$dx = \text{thickness differential} [\text{cm}]$$

The effective conduction distance using the power values for posterior 2°C elevation can be estimated by rearranging the terms of equation (1) and solving for dx :

$$dx = \frac{A k (dT)}{Q} \quad (2)$$

Where,

$$A = 74 \text{ cm}^2$$

$$k = 0.0046 \frac{\text{W}}{\text{cm} \cdot ^\circ\text{C}}$$

$$dT = 2 ^\circ\text{C}$$

$$Q = 3.1454 \text{ W (for } 2^\circ\text{C elevation)}$$

then, the effective conduction distance is $dx = 2.16$ mm, which is sufficiently smaller than the can surface radius of 6 mm.

Conservatively, only the internal (e.g. Upper Inner Can) temperature information should be used for estimating allowed continuous heat. However, both anterior and posterior measurements at the device/skin interface suggest that the body is so efficient and effective at removing heat that the heat input to the can may be doubled and still not exceed the intended temperature increase limit of 2°C. To allow for a safety margin, it could be suggested that the inside temperature rise of the can be limited to 3°C after 8 weeks implantation. This is further justified by the graph of Figure 6 which suggests that heat dissipation from the endogenous source rises chronically. The intersection of the least squares fit line and the 3°C internal temperature rise is approximately 1.3 Watts.

Since the estimate for the effective conduction distance is smaller than the can radius (as demonstrated above), it may be suggested that even the curved surfaces of the simulants function essentially as flat surfaces. Thus, heat removal from the can of an AIMD with dimensions of typical implantable pulse generators (surface area >35 cm²) enclosed in titanium cans is therefore approximately directly proportional to the surface area of the can. A generalized estimate can then be proposed for the power (in W) that can be dissipated by such an AIMD with external surface area A [cm²] for an allowed internal temperature rise $\Delta T_{internal}$ (in °C):

$$P = 0.00606 A \Delta T \text{ [W]} \quad (3)$$

where the constant of 0.00606 [W/cm² °C] is obtained from the average of the temperature/power relationships derived experimentally for the inside of the simulants (upper and lower inner thermocouple data = 2.23 °C/W) and the 74 cm² can surface area of the simulants.

One could consider the lower practical limit of can size for estimating heat loss through this approximation to be 8 mm thickness and 8 cc in volume. The thickness is based on a radius twice the estimated conduction distance (~2 mm). Creating a flat, circular device of 8 mm thickness with a rounded edge, and adding the criterion that the flat surface area is approximately equal to the rounded edge surface area, gives a volume of approximately 8 cc with a 3.75 cm diameter. This device would have diameter to thickness ratio of 4.69.

The upper practical limit of can size for estimating heat loss with this equation would seem to be limited more by the diameter to thickness ratio than the size. As such, the approximation is deemed to be appropriate for a device diameter/device thickness ≤ 10 with no upper device size limit.

VI. CONCLUSION

A series of animal experiments has been performed to obtain data relating endogenous heat generation by an AIMD to temperature increase at the device/tissue interface. A simple technique was presented for estimating the limit of *in-vivo* heating of an AIMD that complies with the 2°C temperature increase limit of the EN 45502-1 standard.

REFERENCES

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TABLE

Thermocouple Location	2°C ΔT elevation
Upper and Lower inner can	0.897 Watts
Anterior and Posterior outside can	2.235 Watts

Table 1 – Estimated endogenous heat that results in a 2°C temperature rise for an AIMD enclosed in a titanium can of area of 74 cm² and volume of 34 cm³.

FIGURE CAPTIONS

Figure 1 – Each simulant comprises a deep-drawn titanium enclosure fitted with four $5\ \Omega$ resistors set inside a machined aluminum block with thermal grease for good thermal conduction. 5 thermocouples measure temperature inside the can, at the device/tissue interface and ~ 2 cm away from the simulant.

Figure 2 - Finished simulant. A silicone rubber tube was placed over the external thermocouples to assure biocompatibility with tissue. The outer thermocouple was adhered to the can with silicone rubber adhesive. The very top of the can had approximately 4 mm thick layer of silicone rubber adhesive over the epoxy. This silicone rubber top was not included in the surface area calculation due to the insulating properties of the silicone rubber.

Figure 3 - Typical temperature data plot for week 1.

Figure 4 - Typical temperature data plot for week 8.

Figure 5 - Composite plot of all temperature increases versus power for all animals. (a) All data points, (b) inner and device/tissue interface temperatures with trend lines.

Figure 6 - Typical average power needed to increase simulant temperature by 2°C as a function of time from implant.

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FIGURES

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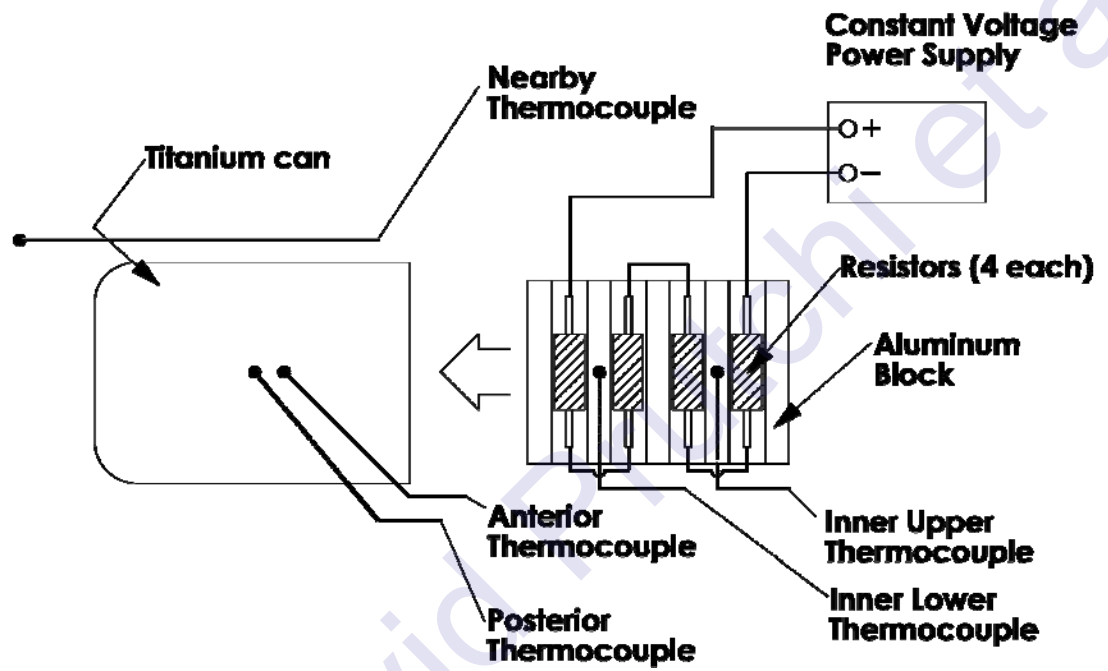


Figure 1



Figure 2

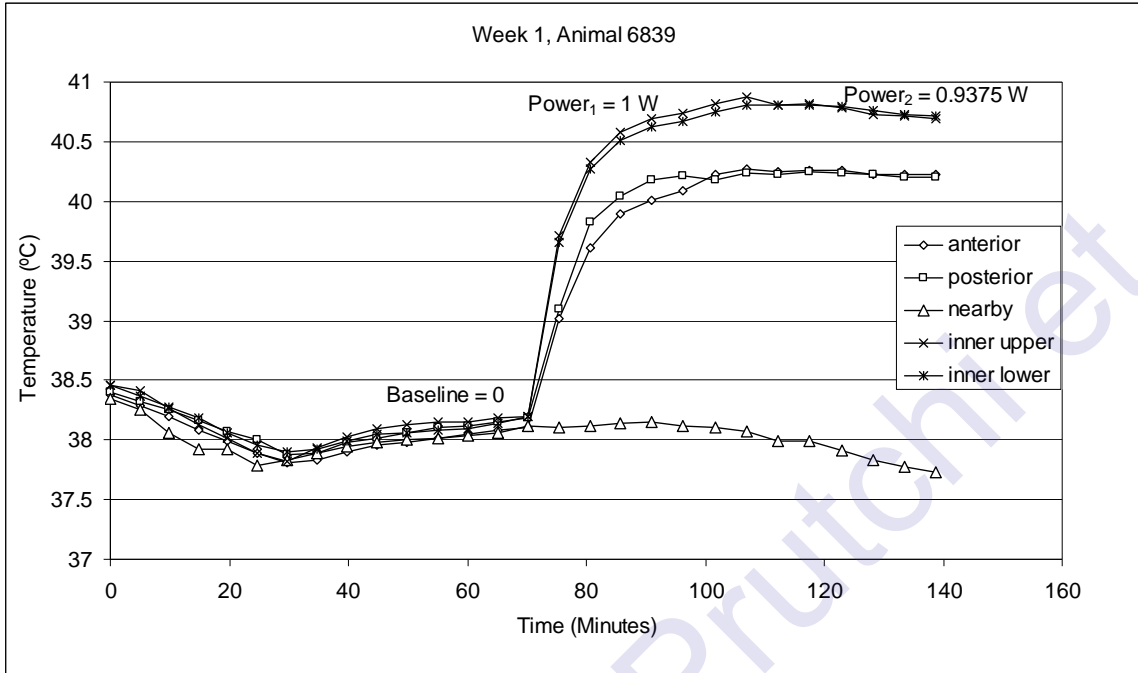


Figure 3

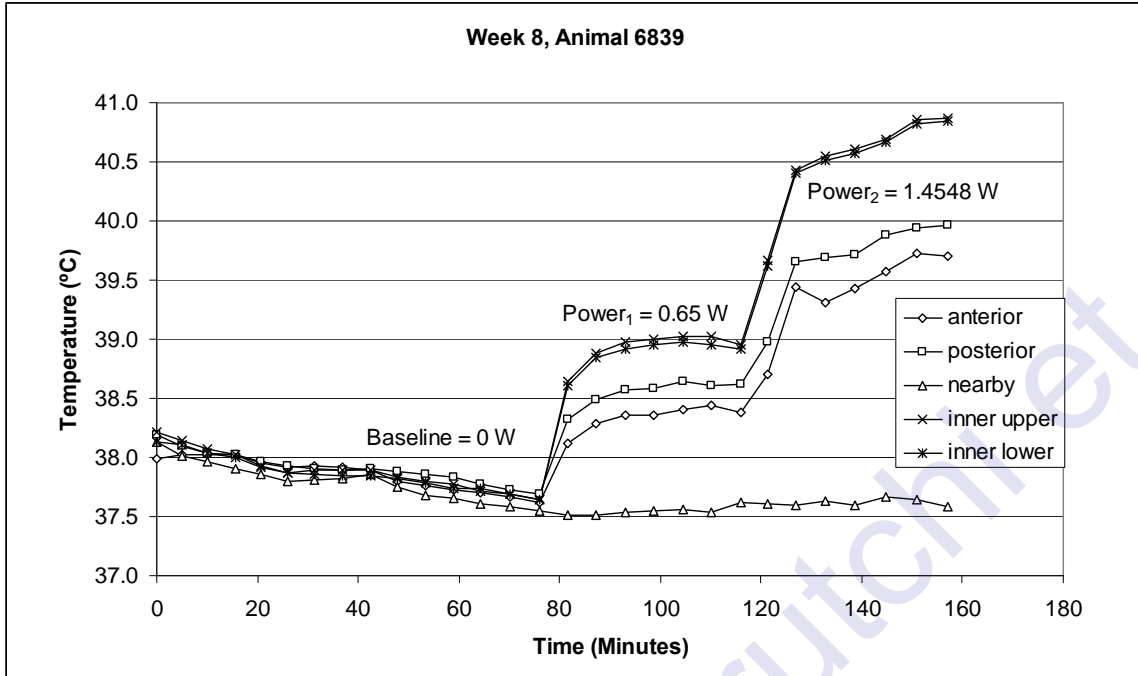
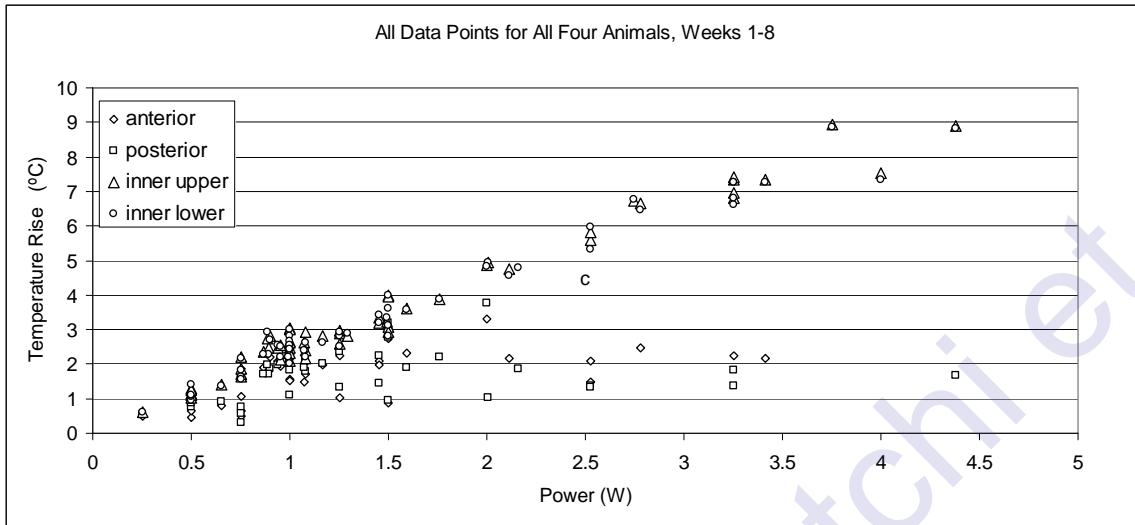


Figure 4

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(a)



(b)

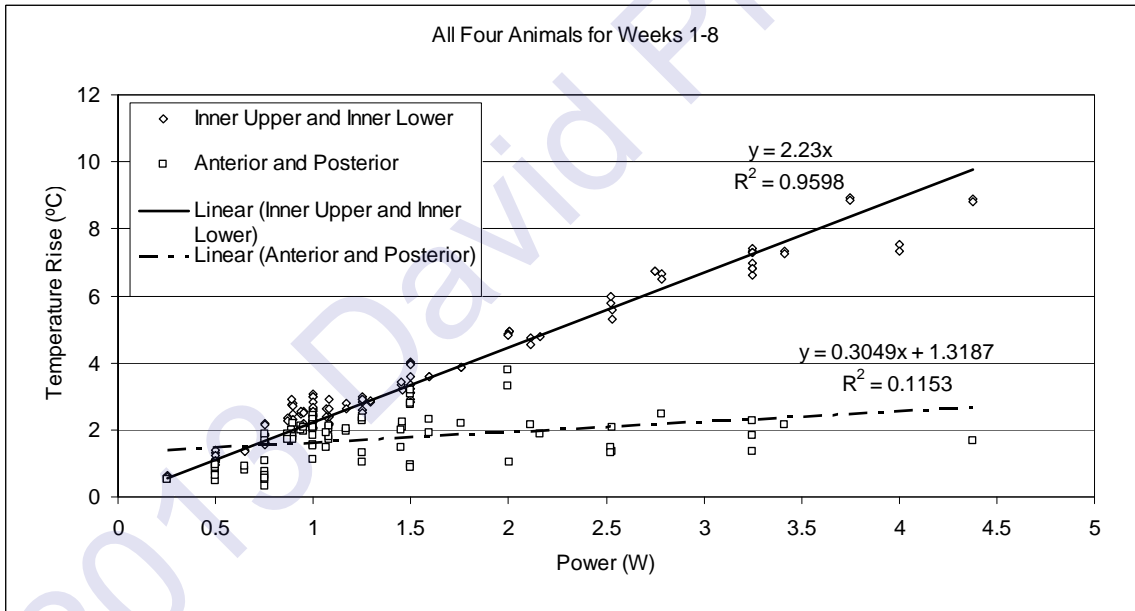


Figure 5

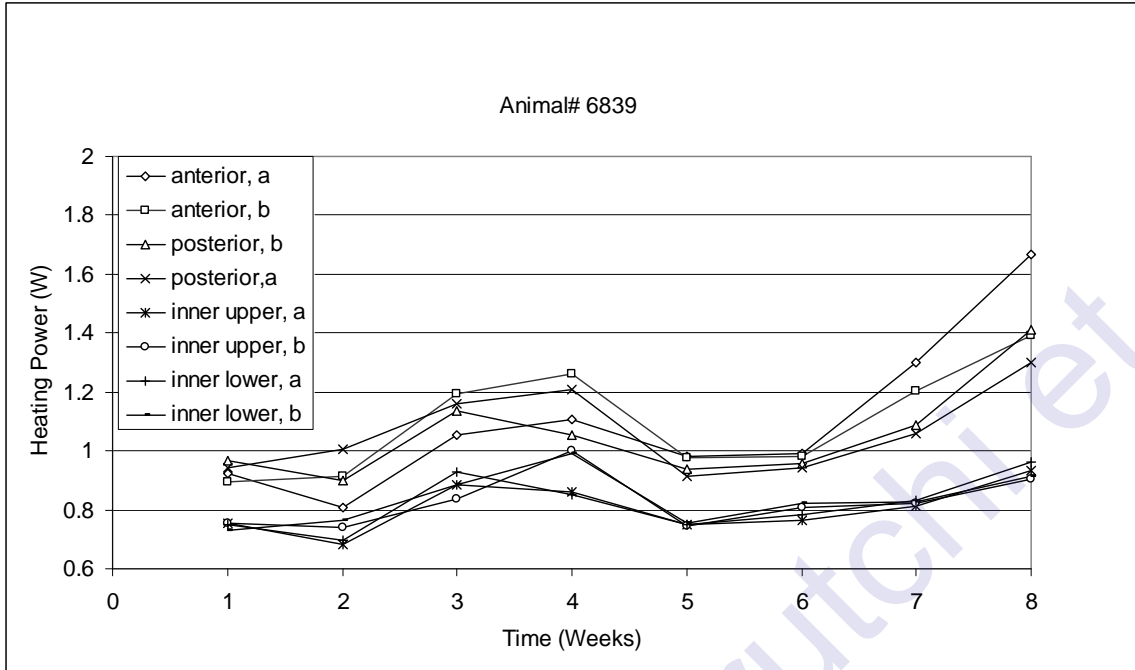


Figure 6

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