Improvements to Heating Device for µPET/CT Machine

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Abstract

Medical imagers require small animals to be anesthetized for up to an hour to ensure their lack of motion during testing. Under anesthesia these animals, oftentimes mice, are subject to a significant decrease in body temperature that can lead to hypothermia or death. During the spring semester of 2007, a heating device was designed in order to provide warmth to mice during μPET/CT scans at temperatures above which hypothermia occurs. The device consisted of a low-flow air pump transporting air through a tube heater .

Problem Statement

Anesthesia slows metabolism, which can lead to hypothermia and eventual death. During prolonged MicroPET/CT scans, small animals, often mice, are exposed to anesthesia for extended periods of time and it is important for the well-being of the animal and the sake of the research to keep the body temperature steady. Heating lights are often used to provide heat but they don't have the capacity to distribute heat uniformly or regulate temperature. Therefore, a heating device was designed in order to provide controllable and steady temperature during prolonged MicroPET/CT scans. The goal is to improve the device to make it more user-friendly and aesthetic and to perform extensive testing.

Motivation

A decrease in the test subject's body temperature during µPET/CT scans has a number of implications. Most notably, temperature loss could lead to hypothermia or even death over the course of an hour-long scan. Aside from the fact that this may violate guidelines on the proper treatment of lab animals during research, it also causes serious setbacks for researchers. Researchers invest a significant amount of time and money implanting and developing specific cancers in these mice and devising treatment plans for the cancer. Death of a test subject may prevent a researcher from making significant contributions to the field of cancer research. In addition, varying body temperatures during a scan and between scans leads to inaccurate and inconsistent images. A heating device capable of providing constant temperature to the mouse would solve these problems and aid in the efficiency of current cancer research.

Client Requirements

The µPET/CT heating device must fulfill four major requirements along with a number of secondary requirements defined by the client. The first main requirement of is that a controllable and uniform temperature must be provided to the mouse inside of the µPET/CT machine. The device will have to produce a final temperature of near 36.9°C, the body temperature of a mouse [5]. The second main requirement is that no metal parts can be located within the µPET/CT machine's field of view while a scan is taking place. Metal parts cause distortions known as artifacts and as the CT revolves 360 degrees around the subject, metal anywhere in the machine will make it difficult for the researcher to analyze the image. The third main requirement for the device is that it must not create potential to harm the µPET/CT machine because this machine is extremely expensive and is the only one in existence. The fourth main requirement for the device is that the cost of production must be under $500.

The device should have minimal movement inside the µPET/CT machine. Too much movement inside the machine's field of view can distort the image. The portion of the device that delivers heat to the mouse must fit inside the µPET/CT imaging chamber which has a circular opening with a diameter of ten centimeters. The last requirement for this device is that it must be cleanable because the mice may urinate during scans. This not only increases sanitation, but prevents the possibility of leaving traces of radioactive isotopes as urine may become radioactive with the radiopharmaceuticals that must be delivered to the mouse for PET scans.

Background Information

PET/CT Imaging

μPET/CT is a machine that combines the technology of PET and CT imaging into one process. The μPET/CT scanner that will house the designed heating device is a product of Siemens and is currently the only operable combined μPET/CT scanner in the world. The PET portion machine provides the necessary information on cellular activity while the CT portion of the machine provides information on the anatomy of the subject. The PET data, when overlaid with a CT scan, creates a complete image of the cancerous cells within the anatomy of the host, as shown in Figure 1.

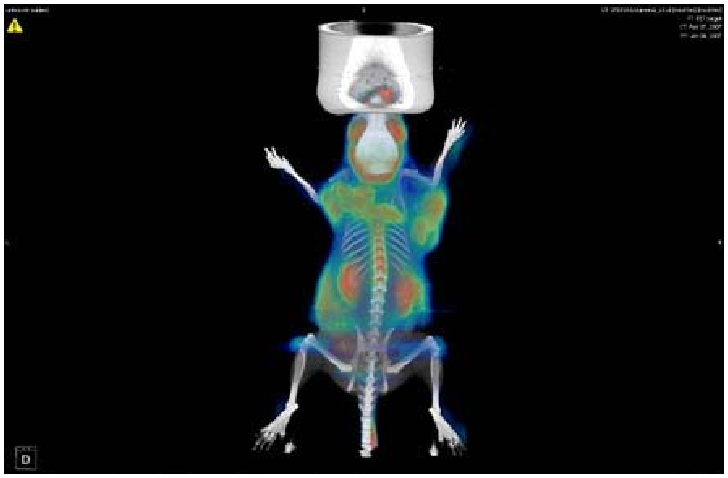

Figure 1. *A μPET/CT image*: This is an image of a mouse provided by this project's client Dr. Robert Jeraj.

PET or Positron Emission Tomography is a nuclear medicine imaging technology that utilizes positron labeled molecules to measure the intensity and function of biological processes without disturbing the test subject [6]. Prior to a scan the subject is injected with a radiopharmaceutical or tracer, often fluoro-2-deoxyglucose which is an analog of glucose. The radiopharmaceutical travels throughout the body by way of the blood stream. This tracer is consumed by the subject's cells through normal metabolic processes. As the tracer molecules begin to decay by means of these cellular processes they emit positrons which are the antimatter counterpart to electrons. When positrons are emitted they almost instantaneously collide with electrons in a process known as annihilation. The byproduct of this annihilation is a pair of gamma rays which travel in opposite directions until they are detected by a scintillator material. The detection allows the machine to pinpoint the location where the annihilation took place, and through the compiling of thousands of these annihilations create an image. PET images represent the relative activity of the cells. In PET images, cancerous areas show up as bright spots on the image due to their increased metabolic activity [1]. Increased metabolic activity in cancer cells is a result of the uncontrolled cell division that characterizes these cells. Using PET imaging, researchers are able to study the growth of cancerous tumors as well as metastasis, the movement of cancer throughout the body.

CT, or Computed Tomography, is an imaging procedure that uses a series of x-rays to create a three dimensional image of the anatomy of a subject. In computed tomography, x-rays are emitted in a single plane. The CT machine measures the attenuation of the different tissues in the body of the subject by sending these x-rays through the body and then collecting them on the opposite side [10]. CT machines are capable of detecting a difference in tissue density as small as 1%. A large number of two dimensional images known as slices are taken around a single axis of rotation. They are then compiled through a number of techniques, most notably tomographic reconstruction, to create a three dimensional image.

PET/CT imaging is widely used as a technique to track the progress of cancer as well as the effectiveness of cancer treatment plans. Throughout the country, clinical machines are used to provide doctors with useful information about their patient's disease. μPET/CT is a smaller version of the machine with a higher resolution, on the scale of microns, compared to the resolution, on a scale of millimeters, of the clinical machine. This increased resolution is necessary to image small animals for research purposes. PET/CT imaging combines the power of the two previously used techniques to provide a more detailed and beneficial image.

Heat Loss of the Mouse

Due to the large surface area to mass ratio of mice as well as their incredibly high metabolic rate, mice lose heat more rapidly than larger animals [2]. As mentioned before, during hour long μPET/CT scans mice can experience hypothermia or even death due to the anesthetic. Anesthesia causes heat loss by sedating the mouse and eliminating muscle activity, a major source of heat production. In addition, under anesthesia, there is a general core to peripheral heat transfer resulting in a substantial heat loss to the environment [3]. The inability to control body temperature is intensified in nude mice that are given this name due to their lack of hair. Nude mice are commonly used in medical research because they possess an inability to reject tumors or transplants of cells from other specimens including humans. This inability to reject foreign cells comes from the absence of a thymus in their body, and, in turn, an absence of T-cells. T-cells are necessary for the immune system to destroy foreign cells that invade the body [8]. Dr. Robert Jeraj uses nude mice to study cancer treatment by first implanting cancerous cells in the mice and then tracking the progress of certain treatment plans using medical imaging techniques such as μPET/CT.

Current Design

The three main components of last semester's design are the mouse enclosure, the heater, and the air pump.

Mouse Enclosure

The mouse enclosure, shown in Figure 2, features a two-chamber system which has multiple benefits. In the two chamber system, heated air (heated by the heater described in the following section) is pumped into the bottom chamber. As a result, the bottom chamber will heat which will heat the platform that divides the top and bottom chamber of the mouse enclosure. Mice will lie on the platform in the top chamber. Thus,

Figure 2. *Mouse enclosure*: An image of the mouse enclosure from last semester's design.

as the platform is heated, the mouse will be heated which will keep the mouse's body temperature within the normal range. Anesthesia will be pumped through the top chamber to keep the mouse anesthetized throughout the procedure. It is beneficial to not have heat pumped through the top chamber because this avoids the possibility of the mouse drying out during the procedure. Furthermore, since a nose cone is not used to keep the mouse anesthetized, multiple mice could potentially be put in the top chamber which would allow for a nice comparison between two mice for our client. The last major advantage of this system, is that the platform is removable. This allows for easy cleaning of the platform as well as the entire enclosure. This is necessary because the mice occasionally urinate during scans. The next major component of last year's design is the heater.

Heater

The heater which was designed last semester utilizes nichrome wire, a thin PVC tube, and a DC power supply. The entire device is shown in Figure 3.

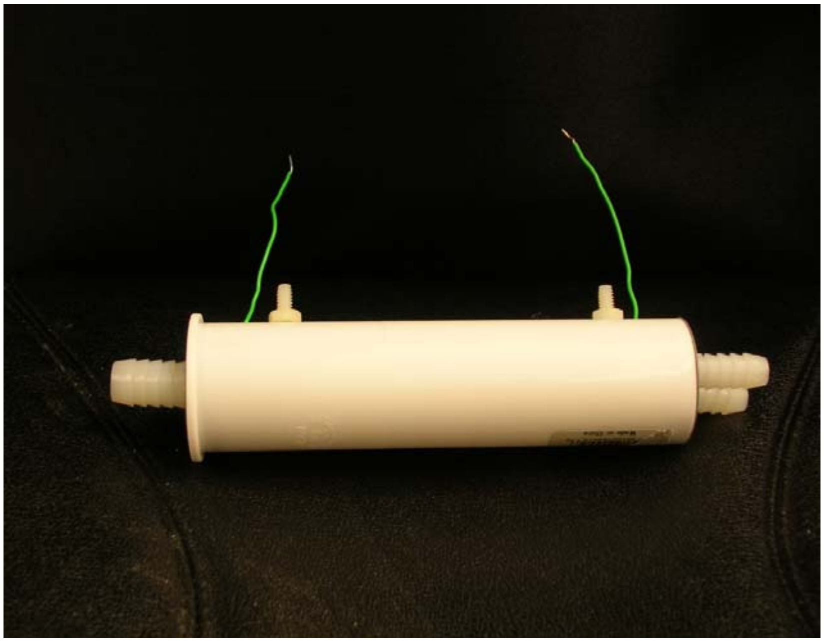

Figure 3. *Heating Apparatus:* This is an image of the heater from last semester's design.

The coiled nichrome wire on the inside of the heater is suspended down the middle of the tube using the two nylon screws which can be seen poking out of the top of the heater in the picture above. Nylon screws were used to avoid conducting heat to the outside of the heater which could have potentially been a problem with metal screws. There are two air inlets which are shown on the right side of the picture. Two inlets were needed because the pump which was purchased had two air outlets. There is a single air outlet on the left hand side which sends the heated air from the heater to the mouse enclosure. Finally, a DC power supply is connected to each of the green wires to apply a voltage over the nichrome wire which will produce a current and ultimately heat. The last major component of last year's design is the air pump.

Air Pump

The air pump that was used is a 100 gallon fish tank air pump which is manufactured by Tetra. A picture of this pump is shown in Figure 4.

Figure 4. *Air Pump:* An image of the air pump from last semester's design.

The air pump has two air outlets (as described previously) which are shown on the left hand side of this picture. The quiet operation of the fish tank air pump was a huge benefit because other air pumps which were considered last semester operated at a high noise level which would be extremely distracting in a lab setting.

Modified Design

Mouse Enclosure

When examining the mouse enclosure, three areas were considered for modifications. First, the wrap-around tube, shown above in Figure 5, was changed from soft vinyl tubing to polyvinyl chloride (PVC). This tube was modified because it continuously became pinched when any pressure was applied and was overall inefficient.

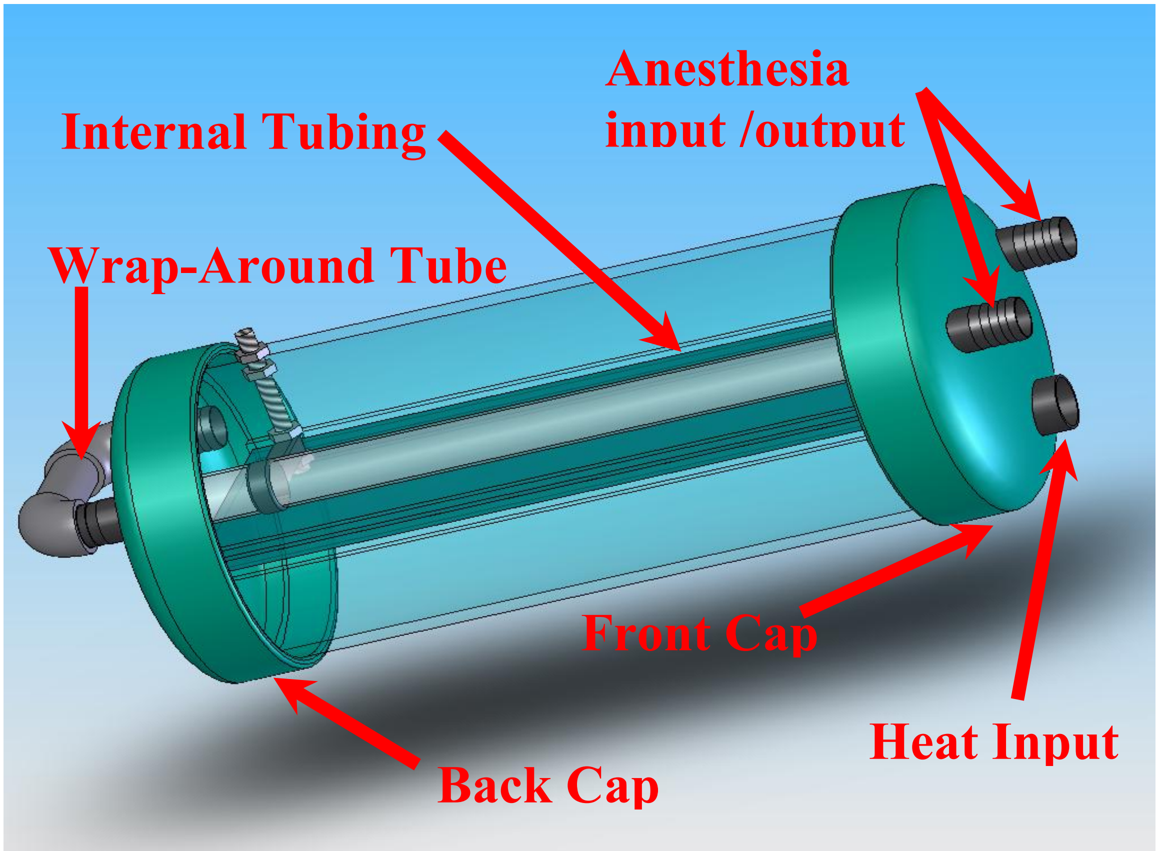

Figure 5. *Mouse Enclosure:* This is an image of the mouse enclosure with the corresponding names of the components.

The wrap-around tube, along with the internal tubing, will serve as a conduit for anesthesia to transport it from the inside of the chamber to a neutralization device. Next, access to the inside of the chamber was relocated to the backside. This modification was proposed since there is only one connection from the back cap to the internal tubing while there are three external tubing connections with the front cap. Accessing the inside of the chamber from the back will allow sealing of the front cap to ensure minimal loss of both anesthesia and heated air to the surrounding area.

Finally, the following design matrix shown in Table 1 was prepared to evaluate the choices considered for improving the platform the mouse will lie on.

Criteria	Weights	Mesh	Polyethylene	Acrylic
Cost	0.1	0.2	0.3	0.1
Conductivity	0.35	1.05	0.7	0.35
Machineability	0.2	0.2	0.4	0.6
Mouse Health	0.35	0.35	1.05	0.7
TOTAL	1	1.80	2.45	1.75

Table 1. *Platform Design matrix*: This table shows the materials as well as the corresponding scores for each criterion.

The three options for material included: a mesh material, a polyethylene material, and an acrylic material. Each of these options was compared using the four criteria of cost, conductivity, machineability, and mouse health. Each of these criteria was given a weight based on the importance of each category to the overall design. Each material was then rated 1, 2, or 3 with 3 being the best in the category, and 1 being the worst in the category. The rating of each material was then multiplied by the weight for the given category. The scores for each material were then totaled. The highest-scoring option that we have is the polyethylene material. Polyethylene has a comparatively high conductivity, allowing for more heat to be transferred to the mouse. The mesh material would have the best conductivity because it is abundant with holes, however, the air transfer would introduce concerns such as drying the mouse and diluting the anesthesia. The polyethylene was chosen as the most beneficial material.

Heater

Several modifications were also considered for the heating apparatus. The first modification to the heater, shown in Figure 6, was to add another nichrome coil.

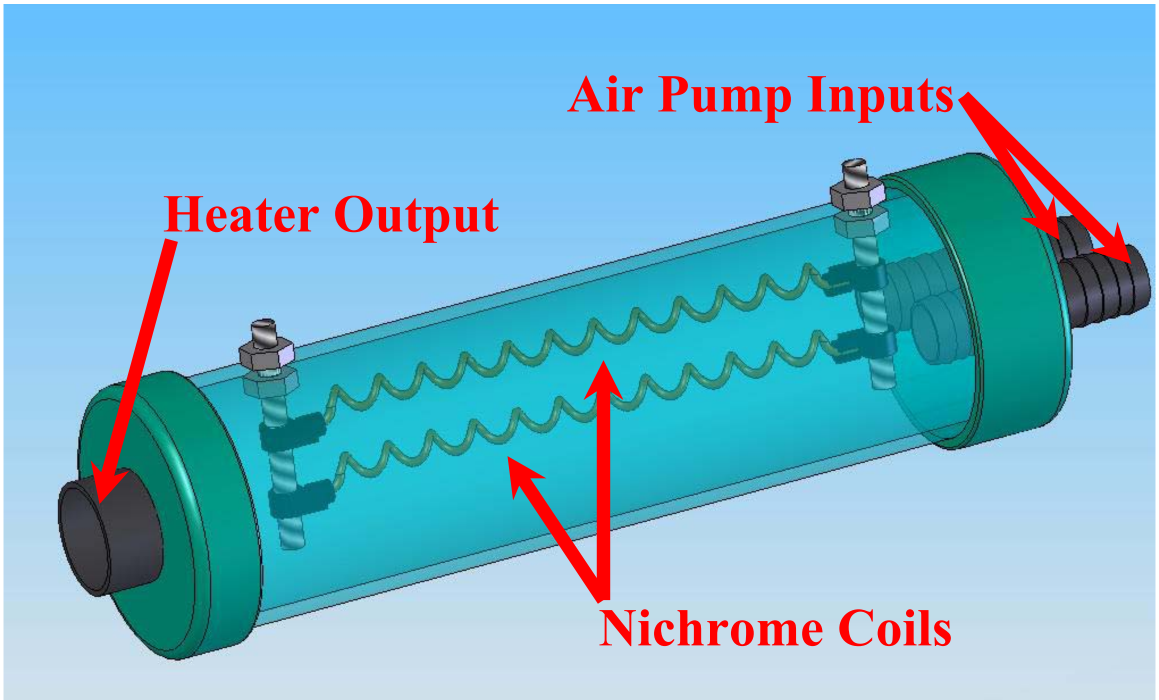

Figure 6. *Heating Apparatus:* This is an image depicting the heater with corresponding components.

This will further increase heat production capabilities when two mice are being simultaneously imaged in the mouse enclosure. In addition, the heater will now have a standard AC (alternating current) power source. This will remove any dependence of DC (direct current) batteries since the device can be directly connected to a standard wall outlet.

Finally, a design matrix shown in Table 2 was prepared to evaluate different options for heater the heater casing to prevent heat loss from the heater.

Criteria	Weights	Thicker PVC	Copper	Thermo-Insulated
Cost	0.1	0.3	0.2	0.1
Insulation	0.6	1.2	0.6	1.8
Machineability	0.3	0.9	0.6	0.3
TOTAL	1.00	2.4	1.4	2.2

Table 2. *Heater Design matrix*: This table shows the materials as well as the corresponding scores for each criterion.

We evaluated the options of thicker PVC tubing, copper tubing, or the use of a thermally insulated material. To compare each of these options, we looked at the three main categories of cost, insulation, and machineability. These were each given a weight, and the materials were rated 1, 2, or 3. The same process followed in the other design matrices was followed to tally the points for each design option. The thicker PVC option was determined to be the best option. PVC is extremely easy to work with which is why it was rated high for machineability. Also, it is extremely cheap which added to the positive characteristics for PVC. We will re-work our heater to use thicker PVC.

Tubing

The design matrix shown in Table 3 was prepared to evaluate different material options to replace the vinyl tubing which is thin and thermally conductive.

Criteria	Weights	Insulation Wrap	PVC	Teflon
Cost	0.2	0.6	0.4	0.2
Insulation	0.5	0.5	1.5	1.0
Machineability	0.1	0.3	0.2	0.1
Durability	0.2	0.2	0.6	0.4
TOTAL	1.00	1.6	2.7	1.7

Table 3. *Tubing Design matrix*: This table shows the materials as well as the corresponding scores for each criterion.

We evaluated foam insulation wrap around the vinyl, PVC and Teflon to determine which would best suit the design. The criteria that were factored into the decision-making were insulation, machneability, durability, and cost. PVC was found to have the greatest insulation properties, is most durable, and is similar in machineability and cost compared to the other two options, making it the best choice for future use.

Final Design

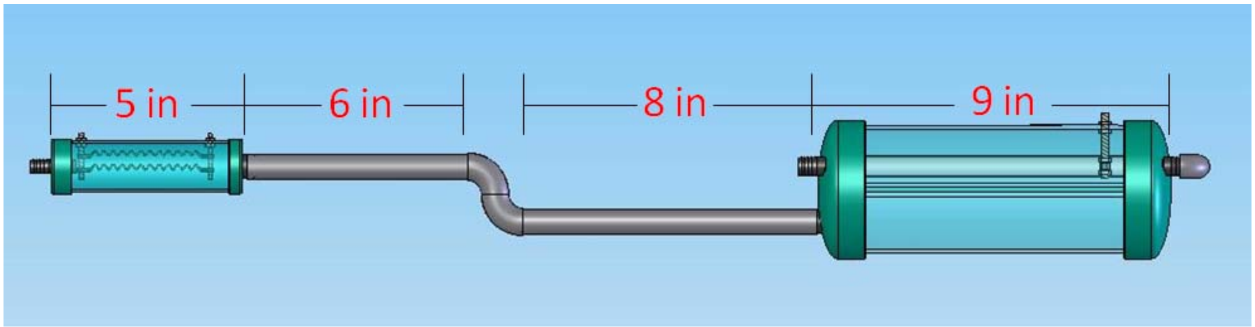

Figure 7. *Entire Device:* An image of the entire device with dimensions.

Figure 7 above shows the entire device with dimensions. An important consideration is that the only components that will be located inside the micro PET/CT scanner are the mouse enclosure and a small section of the PVC tubing. The rest of the tubing and heater will be located in the loading dock casing directly behind the scanner. As a result of an obstacle directly outside the µPET/CT scanner, the heater must be placed on a higher level than the mouse enclosure. An S-shaped connecter will enable us to avoid this obstacle but still use PVC tubing.

Future Work

The main focus of this semester will be to modify and test the device to ensure it transfers the correct heat to the mouse. The first step will be to finish the assembly of the new heater. Nichrome wire will be added to the core of the heater to increase heat production, tube connectors will be added to the caps of the heater to decrease air leakage, and a power supply will be designed to plug directly into a wall outlet for ease of use. Once the production of the heater is complete, testing must be performed mainly to ensure that no parts of the heater melt, and that the temperature production remains constant throughout the duration of use.

Improvements to the mouse enclosure will continue simultaneously as testing is performed on the heater. The current vinyl tubing on the back of the mouse enclosure has kinked, blocking the flow of anesthesia. Thus, the vinyl will be replaced with PVC tubing. Three platform materials, acrylic, .09" thick LDPE, and .12" LDPE, have been purchased but before one is chosen, the maximum output of the heater must be determined as the materials have different thermoconductivities and thicknesses, allowing for different amounts of heat transfer. In preparation for final testing, each material must be cut to size and a row of brackets must be inserted to stabilize the platform. Also, a rubber material will be added to the platform tracks in order to prevent air leaks between the top and bottom chambers.

Lastly, some type of insulation, either the standard foam type or a form of spray-on insulation will be used to insulate the entire outside of the chamber. An important consideration is that the insulation cannot be thicker than ¼”. This size constraint is necessary to ensure that the mouse enclosure will fit in the bore of the micro PET/CT scanner. Overall, the insulation will be used to prevent any conductive heat loss through the walls of the mouse enclosure. Both cost and insulating ability will go into our decision of which material will be used in the final design.

Finally, all of the components of the design must be calibrated and tested. All testing will be repeated three times or until consistent findings are achieved. Using simple heat transfer equations, found in Appendix B, it was determined that 118° F is required at the entrance of the mouse enclosure to maintain the mouse’s body temperature of 96.4° F on the top of the platform. Thus, before the mouse enclosure is complete, the heater can be tested for the temperature output at the end of the PVC tubing connected to the heater. If the output does not reach 118° F, the power supplied to the heater must be increased. If this modification is unsuccessful, the air flow over the nichrome wires will need to be increased, likely requiring replacement of the current pump.

Once the entire system is assembled, testing will be performed in the absence of the mouse and the anesthesia, and temperature will be monitored with a thermometer probe taped to the platform. First, the system will run with the pre-determined power supply to induce an input of 118°F at the entrance of the mouse enclosure. The amount of time it takes for the top of the platform to get reach the body temperature of the mouse, 36.9°C, will be determined. Subsequently, the system will be run for this amount of time added to one hour and fifteen minutes, approximately the maximum amount of time needed for a μPET/CT scan. Temperature will be monitored every five minutes to observe consistency. Finally, the entire system will be tested in the μPET/CT with the employment of anesthesia circulation. If this is successful, the system may then be tested during real scans.

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Appendix A

Product Design Specification: Updated September 23, 2007

Team Members:

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Problem Statement:

During anesthesia, metabolism slows down which can lead to hypothermia and eventual death. For prolonged microPET or microCT scans, where animals are kept for an extended period of time under anesthesia, it is important to keep the animals at steady temperature. Currently heating lights are used to provide a solution, however, these lead to non-uniform and poorly controlled temperature regulation. Therefore, we proposed to design a heating pad that could be used to provide controllable and steady temperature during prolonged scans. Because of the imaging requirements, the heating pad cannot contain metal parts.

Client Requirements:

- Temperature should be close to the body temperature of a mouse
- Temperature should be controllable adjustable?
- The device should provide temperature feedback
- Device should be able to provide heat for roughly one hour

Design Requirements:

- All metal parts must be out of the field of view
- Liquid may be used but if so, device must be completely sealed (no leaking)
- Limit the use of moving parts. Slight motion may be acceptable, but significant motion may destroy image results
- The part of the device that the mouse is sitting on should be somewhat firm so the mouse does not sink into the device

1. Physical and Operational Characteristics

a. Performance Requirement: The device will need to produce temperatures close to the body temperature of a mouse. The output temperatures should be variable and the device should provide live temperature feedback.

b. Safety: The device will likely operate at high temperatures, thus a warning label must be displayed so the consumer uses care during operation. We should use a temperature fuse to automatically turn the device off if the temperature becomes too high. The device will employ a typical electrical plug. Standard safety precautions regarding electrical plugs and outlets should be followed.

c. Accuracy and Reliability: The device should provide variable heat control accurate within 3-5 degrees Celsius of the temperature desired by the operator. Repeatability does not apply as the user will likely make changes to the device during operation.
d. Life in Service: The device should be capable of providing heat throughout the typical length or a microPET/CT scan, about one hour. The device should be able to withstand multiple uses within one day. The product life of the device depends on the working parts used in the design
e. Shelf Life: Shelf life will not likely be an issue with this device
f. Operating Environment: The device will be used at the UW hospital in the room where the microPET/CT scan machine is located.
g. Ergonomics: The temperature control of the device should be straightforward so that the user can easily shift temperature without extensive training. Also, the body temperature of the mouse should be attainable and prominently displayed.
h. Size and Shape: The device must be small enough to fit inside the imaging chamber (4 ¾") of the microPET/CT scanner. The device can be a flat pad, or a design in which the mouse is heated from all sides.
i. Weight: The weight of this device is not of concern.
j. Materials: Features of the device that go inside the imaging chamber cannot have any metal parts. Metal parts may be used on aspects that will not be inside the imaging chamber.
k. Aesthetics, Appearance, and Finish: The device should clearly indicate a warning of the high temperatures the device may produce.

2. Product Characteristics:
a. Quantity: One device is required.
b. Target Product Cost: The prototype should cost less than $500 to build.

3. Miscellaneous:
a. Standards and Specifications: The device should comply with all regulations established by the FDA for medical instruments. More information can be found on the FDA website, http://www.fda.gov/.
b. Customer: The customer for this device will be researchers who desire a more controllable means to keep the body temperature of a mouse constant during imaging.
c. Patient-related concerns: There are no patient related concerns at this time.
d. Competition: Pennsylvania State Bioengineering Team, "Design of a Temperature Controlled Insert for a Microscope Stage." Online: http://www.bioe.psu.edu/SeniorDesignProjects/SD2005/JIfkovits/450Webpage.htm.

Appendix B.

Heat Transfer Equations.

According to the First Law of Thermodynamics, energy must be conserved. Thus,

$$Q_{plate} = Q_{fumes}$$

Where Q_{plate} represents the energy transfer through the surface of the plate and Q_{fumes} represents the energy transfer of the outside of the top half of the mouse house. So,

$$(R_{conduction} + R_{convection}) * (T_{hot\ air} - T_{plate})$$
$$= m_{fumes} * c_{p(fumes)} * (T_{plate} - T_{fumes})$$

$c_{p(fumes)} =$ $thermal\ capacitance\ of\ air + anesthesia \approx 1004\ J/(kg * K)$

$m_{fumes} = mass\ flow\ rate\ of\ air + anesthesia$

$$m_{fumes} = \rho * A * V = v * \rho$$

$$\approx 1.2 \frac{kg}{m^3} * \frac{.05m^2}{s} = .06 \frac{kg}{m * s}$$

$\rho = density\ of\ air \approx 1.2,\ A = cross - sectional\ area\ of\ top\ portion\ of\ tube,$
$V = velocity\ of\ air, v = velocity\ flow\ rate$

$$R_{conduction} = \frac{L}{k * A}$$

where $k = conductivity,\ A = area\ of\ plate\ \ L = thickness\ of\ plate,$

$$R_{convection} = \frac{1}{h * A}$$

where $h = heat\ transfer\ coefficient\ of\ a\ plate,\ A = area\ of\ plate$

Approximations:

$A_{platform}$=3”X7”=0.0135m^2
T_{plate} (desired body temperature of mouse)=36°C
v(fumes and air pump)=.05m/s
$h_{\text{less than 4.572m/s, smooth surface}}$=.99+.21*v=1.00
$k_{\text{Low Density Polyethylene (LDPE)}}$^{1} = .33W*m-1*K-1
L_{1LDPE}=.09”=0.0023m
L_{2LDPE}=.125”=0.00318m
$k_{\text{Polymethylmethacrylate (PMMA, Acrylic)}}$^{1} = .18W*m-1*K-1
$L_{3Acrylic}$=.25”=0.00635m

From Maple, $T_{hot\ air}$ = 118.35°F