Temperature Measurements in Normal and Tumor Tissue of Dogs Undergoing Whole Body Hyperthermia

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ABSTRACT

Temperature was measured in the left ventricle, aorta, liver, brain, lung, bone marrow, kidney, and spontaneous solid tumors in dogs undergoing whole body hyperthermia in a radiant heat device. Rectal temperature was found to be a satisfactory indicator of systemic arterial temperature during plateau temperature conditions but rectal temperature underestimated arterial temperature during heating and overestimated it during cooling. Lung temperature, based on small airway temperature, was the same as rectal temperature during plateau temperature conditions. Liver and brain temperatures were slightly higher (0.1-0.2°C) than rectal temperature during the plateau phase. During plateau temperature conditions, kidney temperature measurements were higher than rectal temperature when one site/kidney was measured but were lower than rectal temperature when two sites/kidney were measured suggesting invasive thermometry may have affected measured temperature values. Tibial marrow temperature was greater than rectal temperature during cooling but fell below rectal temperature during plateau temperature conditions by as much as 1.3°C. Femoral marrow temperature was below rectal during heating but gradually exceeded it during steady state conditions, by 0.1-0.4°C. Temperature in solid tumors was variable, sometimes exceeding (0.6°C) and sometimes being less (1.8°C) than rectal temperature.

INTRODUCTION

Whole body hyperthermia is being investigated as a modality for use in cancer treatment (1-4). Whole body hyperthermia involves elevation of body temperature to approximately 42°C with maintenance at that temperature for periods of time usually between 1 and 4 h. Various methods have been used to elevate body temperature. These include warm water suits (1), hot wax baths (5), warm water blankets (6), extracorporeally heated blood (7), a radiant heat device (8, 9), and an immersion bath method (10).

Whole body hyperthermia is not likely to be effective when used alone but may prove beneficial when used to enhance effects of chemotherapy (4), total body irradiation (4), or local or regional hyperthermia in spontaneous tumors in dogs undergoing whole body hyperthermia in a radiant heat device. Rectal temperature was found to be a satisfactory indicator of systemic arterial temperature during plateau temperature conditions but rectal temperature underestimated arterial temperature during heating and overestimated it during cooling. Lung temperature, based on small airway temperature, was the same as rectal temperature during plateau temperature conditions. Liver and brain temperatures were slightly higher (0.1-0.2°C) than rectal temperature during the plateau phase. During plateau temperature conditions, kidney temperature measurements were higher than rectal temperature when one site/kidney was measured but were lower than rectal temperature when two sites/kidney were measured suggesting invasive thermometry may have affected measured temperature values. Tibial marrow temperature was greater than rectal temperature during cooling but fell below rectal temperature during plateau temperature conditions by as much as 1.3°C. Femoral marrow temperature was below rectal during heating but gradually exceeded it during steady state conditions, by 0.1-0.4°C. Temperature in solid tumors was variable, sometimes exceeding (0.6°C) and sometimes being less (1.8°C) than rectal temperature.

MATERIALS AND METHODS

Seventeen mongrel dogs obtained from the Laboratory Animal Medicine Service, School of Veterinary Medicine, North Carolina State University were used for temperature measurements in the left ventricle, aortic arch, liver, lung, kidney, bone marrow, and brain (Table 1). Mongrel dogs were heated only once and were killed by barbiturate overdose at the end of the heating session. Thermocouple position was documented by postmortem examination. Subsequent histological analysis of brain, liver, kidney, pancreas, lung, bone, bone marrow, myocardium, lymphoid tissue, skin, skeletal muscle, intestine, urinary bladder, and adrenal gland was performed. In 4 dogs, the brain was perfusion fixed with a 1% glutaraldehyde-4% formaldehyde mixture. All other tissues were immersion fixed in 10% neutral buffered formalin. Histological preparations were stained with hematoxylin and eosin and/or Masson's trichrome stain.

Four privately owned pet dogs with spontaneous solid tumors were used for intratumoral temperature measurements.

Food was withheld from all dogs during the 12-h period immediately prior to hyperthermia; enemas were not given. Enemas may result in accumulation of gas and/or fluid in the colon. This condition was felt to be a potentially greater source of variation in colon environment and possibly temperature measurement than was the presence of fecal material.

Whole body hyperthermia was produced in a radiant heat device designed specifically for large animal heating (Enthermics, Inc., Menomonie Falls, WI). The device used for these experiments was a first generation large animal device in which the heating surface was uncoated polished metal. In a later generation of this device, the heating surface was coated with a black emulsion to increase emissivity. Radiant heating methodology and data concerning preliminary use of the radiant heat device have been reported previously (4, 8, 9). A line drawing of the configuration of this device is shown in Fig. 1. Briefly, the device has open ends which can be enclosed, completely or in part, with reflective blankets to control heat loss from the device. In addition, heating elements are thermostatically controlled. The open ends of the device are routinely covered with the reflective blankets during heating, and the blankets are usually raised during plateau temperature conditions. Rectal temperature can be accurately controlled by adjustment

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1 Resources used to support this research were partially provided by the State of North Carolina.

2 To whom requests for reprints should be addressed.
TEMPERATURE MEASUREMENTS DURING WHOLE BODY HYPERTHERMIA

Table 1 Sites other than skin, muscle, s.c., rectum and esophagus at which temperature measurements were made in each dog

<table>
<thead>
<tr>
<th>Dog</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lung</td>
</tr>
<tr>
<td>2</td>
<td>Lung, aorta</td>
</tr>
<tr>
<td>12</td>
<td>Left ventricle, lung</td>
</tr>
<tr>
<td>13</td>
<td>Brain</td>
</tr>
<tr>
<td>14</td>
<td>Brain</td>
</tr>
<tr>
<td>15</td>
<td>Tibia, femur</td>
</tr>
<tr>
<td>16</td>
<td>Tibia</td>
</tr>
<tr>
<td>19</td>
<td>Left ventricle, femur, tibia</td>
</tr>
<tr>
<td>28</td>
<td>Lung</td>
</tr>
<tr>
<td>29</td>
<td>Lung</td>
</tr>
<tr>
<td>33</td>
<td>Liver, kidney</td>
</tr>
<tr>
<td>36</td>
<td>Liver, kidney</td>
</tr>
<tr>
<td>42</td>
<td>Liver, aorta</td>
</tr>
<tr>
<td>43</td>
<td>Liver, kidney</td>
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<tr>
<td>49</td>
<td>Kidney</td>
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<tr>
<td>50</td>
<td>Kidney</td>
</tr>
<tr>
<td>51</td>
<td>Kidney</td>
</tr>
</tbody>
</table>

Temperature was administered i.v. at 10 ml/kg/h throughout the procedure. Lactated Ringer’s solution was administered i.v. at 10 ml/kg/h throughout the procedure. Atracurium was maintained by atracurium infusion (8.5 μg/kg/min) as previously described (18). Total thiopental dose was limited to a maximum of 30 mg/kg during the course of the heating session. Lactated Ringer’s solution was administered i.v. at 10 ml/kg/h throughout the procedure.

After the dogs were anesthetized, ventral abdominal hair was clipped so that it would not interfere with heat transfer. The dogs were then placed on a mesh stretcher in dorsal recumbency and moved into the radiant heat device (Fig. 1). Temperature probes were positioned as follows. One rectal probe was placed through a 1 French red rubber catheter (Rob-Nel Catheter; Monoject, St. Louis, MO) from which the closed end had been removed and sutured to the catheter with the temperature-sensitive portion extending 1 cm beyond the end of the catheter. The rubber catheter provided the stiffness necessary to insert the thermistor to the desired depth of 10 cm.

For liver temperature measurement, a conventional 7 French open-end angiographic catheter was inserted through a femoral arteriotomy and placed in the desired location using fluoroscopic guidance. The thermocouple was then inserted through the angiographic catheter with the temperature-sensitive portion extending just beyond the end of the catheter.

For kidney temperature measurement, the left kidney was surgically exposed through a paralumbar fossa retroperitoneal approach. Temperature was measured at one site near the corticomedullary junction in 4 dogs and at 2 sites, one in the cortex and the other in the medulla, in 2 dogs. In dogs in which temperature was measured at 2 sites, one site was in the cranial pole and the other in the caudal pole. Thermocouples were inserted into closed-end 16-gauge catheters (Inseyl; DeSere Medical Inc., Sandy, UT) which had been inserted into the kidney parenchyma and then sutured to the capsule. Each thermocouple was secured to the catheter with tape. The kidney was returned to its normal location, the proximal ends of the catheter and thermocouple were routed through the incision for access, and the paralumbar incision was closed.

For liver temperature measurement, a conventional 5 French angiographic catheter was wedged into an intrahepatic branch of the hepatic vein by femoral venotomy and fluoroscopic guidance. After the angiographic catheter was secured by ligating it in the femoral vein, a thermocouple was passed through the angiographic catheter until it wedged into a hepatic sinusoid.
Temperature measurements during whole body hyperthermia

Lung temperature was measured by passing a conventional 5 French angiographic catheter distally into the trachea, between the tracheal wall and endotracheal tube, and then into a peripheral bronchus until the catheter became wedged in a bronchiale. The catheter was then retracted 1 cm and secured to the mandible with tape. A thermocouple was then inserted through the angiographic catheter such that the temperature-sensitive tip extended 1.5 cm beyond the end of the angiographic catheter. At this position, the thermocouple tip was not wedged and was located in a respiratory bronchiole with a diameter of approximately 2 mm as subsequently determined by postmortem examination. Pullback thermometry was done after target temperature was reached by pulling the angiographic catheter/thermocouple combination proximally in 5-mm increments allowing for temperature equilibration at each point. Before pullback measurements were taken, 0.5 ml of barium sulfate was injected through the angiographic catheter into the lung in order to identify the exact location of the thermocouple tip at postmortem examination. The exact path of pullback temperature measurements and corresponding airway size could then be easily recorded.

Bone marrow temperature was measured by placing a thermocouple directly into the marrow cavity of either the tibia or femur or both. This was accomplished by first drilling a 3-mm hole through either the distomedial tibial cortex or intercondylar femoral cortex with a Steinman pin. A 16-gauge over-the-needle catheter (Angiocath; Deseret) was then inserted through the drill hole into the medullary cavity. The thermocouple was then inserted into the catheter with the sensitive tip protruding slightly from the catheter end.

For brain temperature measurement, the calvaria was surgically exposed and 2 drill holes were made approximately 1 cm lateral to the midline on the right side overlying the parietal cortex. Rostrocaudal separation of the holes was approximately 2 cm. A 16-gauge over-the-needle catheter (Quik-Cath; Travenol Laboratories, Inc., Deerfield, IL) was inserted through each hole approximately 1.5 cm into the brain. The catheters were secured to the skull and thermocouples were inserted into each one such that the tip of the thermocouple extended to the tip of the catheter. The scalp incision was closed leaving the catheters and thermocouples protruding through the incision.

Temperature was measured in spontaneous solid tumors in 4 dogs. Thermocouples were inserted into 16-gauge over-the-needle catheters (indwelling catheter; Monoject) which had been inserted into the tumor. The thermocouple did not extend beyond the tip of the catheter. Depth of catheter insertion into the tumor depended on tumor size. An attempt was made to insert the tip of the catheter into the center of the tumor. Tumors in these 4 dogs were a large soft tissue brachial fibrosarcoma with a volume of approximately 1000 cm³ (2 sites measured), a plaque-like squamous cell carcinoma of the buccal mucosa (2 sites measured), and 2 gingival malignant melanomas each having a volume of approximately 30 cm³ (one site measured in each).

Corrected temperature at the site in question was plotted either as a function of time or, in order to evaluate temperature at a site relative to rectal temperature, the difference between the site and rectal temperature was plotted as a function of time. Individual temperature profiles for each site were examined.

RESULTS

A typical heating profile for a dog in the radiant heat device is shown in Fig. 2. Rectal and esophageal temperature increased steadily until rectal temperature reached the target temperature of 42°C. Heating rate for all dogs in this project was approximately 0.04–0.06°C/min.

In order to determine if rectal temperature was a satisfactory indicator of systemic arterial temperature, the difference between systemic arterial and rectal temperature was plotted as a function of time (Fig. 3). Systemic arterial temperature was greater than rectal temperature during the heating phase of whole body hyperthermia but during the plateau phase they were essentially equal. During the cooling phase, arterial temperature decreased more rapidly than rectal temperature (data not shown). Temperatures measured in brain and liver were similar (Figs. 4 and 5). In general, temperature in these organs was higher than rectal temperature during heating. During the plateau phase of heating, liver and brain temperatures were slightly higher (0.1–0.2°C) than rectal temperature.

Lung temperature measurements were similar in all 5 dogs. A typical plot of temperature as a function of pullback distance during the plateau phase of heating is shown in Fig. 6. It appears that deep lung temperature is equal to rectal temperature during the plateau phase of whole body hyperthermia. In the more proximal and larger airways, temperature decreases and fluctuates.

Temperatures measured in kidney, bone marrow, and in
spontaneous solid tumors were different from rectal temperature during whole body hyperthermia. Kidney temperature in dogs in which temperature was measured at one site near the corticomedullary junction was greater than rectal temperature during heating and plateau phases (Fig. 7). In dogs in which kidney temperature was measured at 2 sites, one in the cortex and one in the medulla, kidney temperature was less than rectal temperature during the plateau phase (Fig. 8).

Bone marrow temperature appeared to depend on the anatomic location and morphology of the bone in which temperature was measured (Fig. 9). In this project the tibia and femur were studied. The tibia is smaller than the femur and has comparatively little muscular covering. From Fig. 9 it is apparent that tibial bone marrow temperature was greater than rectal during heating by 0.4–1.3°C but fell below rectal temperature by as much as 1.3°C during the plateau phase. Femoral temperature, conversely, was lower than rectal during heating but gradually equaled and slightly exceeded (0.1–0.4°C) rectal temperature during the plateau phase.

Temperature in solid tumors during whole body hyperthermia was found to be variable, sometimes exceeding and sometimes being less than rectal temperature in the heating and plateau phases of the whole body hyperthermia treatment (Fig. 10).

Histopathological analysis of tissue taken at postmortem examination revealed the following changes. In the brain, there was generalized dilatation of the subarachnoid space in 3 of 4 brains studied. The subarachnoid space was often filled with an eosinophilic proteinaceous fluid compatible with edema. The only other change seen in the brain was associated with placement of thermocouples. Those changes included a small amount of subdural and parenchymal hemorrhage and malacia surrounding the thermocouple tract. In one dog the area of hemorrhage and malacia around the thermocouple tip was 5–7 mm diameter. Subdural and subarachnoid hemorrhage occasionally extended approximately 1.0–1.5 centimeters from the point of thermocouple insertion. Liver generally demonstrated a mild...
TEMPERATURE MEASUREMENTS DURING WHOLE BODY HYPERTHERMIA

![Graph showing temperature measurements during whole body hyperthermia.](image)

**Fig. 10. Intratumoral temperature minus rectal temperature as a function of time at 6 sites in 4 dogs undergoing whole body hyperthermia.**

- **Dog 37:** brachial tumor.
- **Dog 17:** oral tumor.
- **Dog 37:** oral tumor.
- **Dog 18:** left oral mucosal tumor.
- **Dog 37:** oral tumor.
- **Dog 23:** oral tumor.

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**DISCUSSION**

Dogs in this project were under general anesthesia for whole body hyperthermia. Use of general anesthesia for whole body hyperthermia permits more aggressive control and support of patient reflexes, fluid requirements, and blood gases (19). Control of ventilation by means of neuromuscular blocking agents such as atracurium prevents heat-induced hyperventilation and respiratory alkalosis during whole body hyperthermia, and in dogs also prevents heat loss via their effective panting mechanism (20, 21).

The use of mechanical ventilation during general anesthesia has been suggested as being a possible cause of reduced hepatic blood flow thereby making the subject prone to hyperthermia-induced liver failure (22). We have monitored various biochemical parameters of liver damage in older pet dogs with spontaneous tumors treated with whole body hyperthermia as described herein and found transitory increases in serum alkaline phosphatase but this returned to baseline values within 7 days and permanent evidence of liver damage was not found.3 In addition, evidence of vascular congestion was not found when livers from the mongrel dogs were examined microscopically. Thus, we have not identified significant pathophysiological complications associated with the use of mechanical ventilation in whole body hyperthermia.

Some investigators have used an in-line heater in the airway of anesthetized dogs undergoing whole body hyperthermia and have observed that this increases esophageal temperature (14). In addition, this was thought to be of potential benefit in assuring that intrathoracic temperature was equal to that in other parts of the body (14). Use of an in-line airway heater may be of benefit in increasing esophageal and major airway temperature but data presented in this paper support small airway temperature being equal to systemic arterial temperature during the plateau phase of whole body hyperthermia without use of an in-line airway heater.

The heating profile illustrated in Fig. 2 is typical of those observed for all dogs treated in this project. After the dog was placed in the radiant heat device, rectal temperature rose steadily to the target temperature of 42°C where it was maintained for the duration of the plateau phase of the treatment. Esophageal temperature was routinely lower than rectal temperature presumably because of the cooling effect of air in the adjacent trachea.

In whole body hyperthermia, body temperature is often referred to as “core” temperature. The concept of core, however, is not supported anatomically as there is no identifiable homogeneous core structure in which measured temperature can be used to estimate systemic thermal dose. Therefore, we measured rectal temperature in all dogs and compared it to temperatures measured at other sites, in an attempt to determine if temperature measured at this readily accessible site was a satisfactory indicator of temperature at other, deeper, less accessible, sites.

One question that we wished to address was whether rectal temperature was a satisfactory indicator of systemic arterial temperature during whole body hyperthermia. Relative to this point, we measured systemic arterial temperature in either the left ventricle or aorta. When aortic or left ventricular temperature was compared to rectal temperature (Fig. 3) it was apparent that arterial temperature was higher during heating but was essentially equal to rectal temperature during the plateau phase of the treatment. During cooling, systemic arterial temperature decreased more rapidly than rectal temperature. We interpreted the increased systemic arterial temperature during heating to be due to intravascular distribution of superficially absorbed heat. This would not be reflected immediately in rectal temperature. The more rapid drop in systemic arterial temperature than rectal temperature during cooling probably reflects superficial heat loss which would be detected within the vascular system before the rectum. Therefore, it appears that rectal temperature is a satisfactory indicator of systemic arterial temperature during the plateau phase of whole body hyperthermia but that during the heating and cooling phases, rectal temperature does not accurately reflect systemic arterial temperature.

Temperatures in brain and liver were higher than rectal temperature during heating by approximately the same magnitude as was systemic arterial temperature. Thus, increased liver and brain temperature during heating was probably a reflection of the temperature of arterial blood supply to these organs. In addition, brain and liver temperatures were slightly higher (0.1–0.3°C) than rectal temperature during the plateau phase of heating (Figs. 4 and 5). One possible explanation for this slight increase in liver and brain temperature over that recorded in the rectum is metabolic heat production. Both organs are metabolically active and metabolic heat production (23, 24) augmented by the hyperthermic state could conceivably result in such differences.

Increased liver temperature in relation to rectal temperature during whole body hyperthermia has been previously reported in rats (16) and in pigs (15). In rats the theory was proposed that the elevated liver temperature was possibly due to decreased hepatic heat transfer due to congestion (16). In pigs, no reason for the increased hepatic temperature was hypothesized (15). In dogs in this study, no evidence of liver congestion was found.
Therefore, metabolic heat production seems to be a more plausible explanation.

Brain temperature during whole body hyperthermia is of interest stemming in part from previous reports of electroencephalogram changes and convulsions observed in human patients undergoing whole body hyperthermia (6, 25). Brain temperature has been measured by others in dogs and pigs undergoing whole body hyperthermia. In one study in dogs, cerebral temperature was found to be 0.3–0.4°C higher than rectal temperature, with slight differences recorded between left and right sides (17). In other studies in pigs (15) and dogs (14), no difference was found between brain and rectal temperature during whole body hyperthermia. In another study in dogs, brain temperature was found to be 1.4°C lower than rectal temperature (26). It is difficult to compare available brain temperature data because of differences in depth of measurement, whether unilateral or bilateral measurements were made, differences in method of anesthesia, differences in body position during heating, and differences in method of heating. Although more work needs to be done to clarify the significance of these variables, most data, including those reported herein, suggest that brain temperature may be slightly (0.1–0.4°C) greater than rectal temperature during the plateau phase of whole body hyperthermia. This increased brain temperature may be due to metabolic heat production.

Histologically, an increase in size of the subarachnoid space surrounding the brain and evidence of increased fluid content therein was found in 3 of 4 brains studied. Since these dogs were killed immediately after hyperthermia and brain electrical activity was not monitored during hyperthermia, the significance of this finding is unknown.

During the cooling phase, neither brain nor liver temperature remained above rectal temperature as one might expect if metabolic heat production in these organs was significant. However, we have shown herein that rectal temperature lags behind systemic arterial temperature during heating and cooling. Thus, brain and liver temperature may have remained elevated relative to arterial temperature because of metabolic heat production but we were not able to document this since arterial temperature was not measured in all dogs.

Lung temperature was evaluated by measuring airway temperature using a pullback technique. All temperature profiles were similar (Fig. 6). These data suggest that lung temperature, based on airway temperature in a 2-mm diameter airway and proceeding 2 cm proximally, is equal to systemic arterial temperature during the plateau phase of whole body hyperthermia. In larger and more proximal parts of the airway system, airway temperature decreases and fluctuates with respiration. As stated previously, dogs in this experiment were under general anesthesia and were mechanically ventilated without use of an in-line airway heater. Based on our data, use of an in-line heater is not necessary in order for lung parenchyma to be heated to systemic arterial temperature at the corticomedullary junction (Fig. 8). Kidney temperature in these dogs was greater than rectal temperature during heating presumably due to the increased temperature of incoming arterial blood (Fig. 3). During the plateau phase, kidney temperature remained higher than rectal temperature by 0.1–0.4°C (Fig. 8). We interpreted this effect as possibly being due to metabolic heat production within the kidney. In additional experiments, we measured kidney temperature at 2 sites in 2 dogs (Fig. 9). Temperature measurements were different from dogs in which temperature was measured at only one site. We found that temperature during heating was lower than rectal temperature at all sites at the start of the heat procedure. During the plateau phase, temperature at all sites was equal to or lower than rectal temperature by as much as 0.3°C (Fig. 9). These data are consistent with reduced renal blood flow in dogs in which temperature was measured at 2 sites in relation to dogs in which temperature was measured at only one site. If renal blood flow was reduced, temperature would be decreased during heating since heat is distributed during whole body hyperthermia by blood flow (Fig. 3). Under these circumstances, kidney temperature would remain lower than rectal temperature because renal metabolic activity and associated metabolic heat production would likely be decreased as a result of the decreased renal blood flow. The hypothesis that renal blood flow was reduced in dogs in which temperature was measured at 2 sites is supported by the postmortem finding of an extremely pale-appearing experimental kidney in comparison to a normal-appearing contralateral control kidney in one of these dogs. Further studies have been initiated to elucidate this question. Renal temperature and intrarenal temperature distribution during whole body hyperthermia are extremely important because it is likely to have a dramatic effect on degree of nephrotoxicity seen as a result of hyperthermic enhancement of action of nephrotoxic agents such as cisplatin (27).

Bone marrow temperature was measured in 3 dogs. The resultant temperature profile depended on whether temperature was measured in the tibia or femur (Fig. 9). Temperature in femoral bone marrow was lower than rectal temperature during heating but equaled and then exceeded rectal temperature at some time during the plateau phase. Temperature in the tibial bone marrow was greater (0.4–1.3°C) than rectal temperature during heating but was lower than rectal temperature by as much as 1.3°C during the plateau phase. Bone marrow in the tibia, a superficial bone without heavy muscular covering, seemingly behaves as a superficial tissue (e.g., skin; see Fig. 2) being subject to direct heat absorption during heating when ambient temperature in the radiant heat device is high and to direct heat loss during the plateau phase of heating when temperature in the radiant heat device decreases. This is supported by the fact that during cooling, tibial bone marrow temperature decreased more rapidly and to a lower absolute temperature than did femoral bone marrow temperature (data not shown). In addition, the femur is surrounded by a large muscle mass which may serve as an insulator and thereby prevent heat loss during the plateau phase of heating where temperature in the radiant heat device drops. In a previous report of tibial bone marrow temperature measurement in pigs (15), bone marrow temperature was found to be less than rectal temperature during the plateau phase of heating. This agrees with data reported herein. However, in our study, kidney temperature during whole body hyperthermia has been measured previously in pigs (15) and dogs (14) and has been found to be the same as rectal. In our study, kidney temperature depended on whether temperature was measured at one or 2 sites (Figs. 8 and 9). Our initial experiments involved temperature measurement at one site near the corticomedullary junction (Fig. 8). Kidney temperature in these dogs was greater than rectal temperature during heating presumably due to the increased temperature of incoming arterial blood (Fig. 3).
because of temperature differences. In other words, regions such as tibial bone marrow may be sanctuaries for residual cancer since thermal effect during the plateau phase of heating will be less than in regions such as femoral bone marrow. On the other hand, temperature in regions such as tibial bone marrow may be high enough during heating to compensate for the decreased biological effect resulting from the lower temperature during the plateau phase. Alternatively, in neoplastic disease where there is no marrow involvement, the lower marrow temperature in some bones may serve as a mechanism for providing some degree of protection to marrow stem cells when whole body hyperthermia is combined with myelosuppressive agents.

Temperature was measured at 2 sites in a bulky fibrosarcoma of the brachium, 2 sites in a plaque-like squamous cell carcinoma of the buccal mucosa, and one site in each of 2 gingival melanomas (Fig. 10). Temperature profiles were variable with temperature at some sites being greater than and at other sites being less than rectal temperature during both heating and plateau phases. The variability in temperature distribution does not seem to be a function of tumor size or location. For example, temperature at one site within the brachial fibrosarcoma was higher than rectal temperature whereas at the other site, intratumoral temperature was less than rectal (Fig. 10); also, temperature in one of the gingival melanomas was much lower than rectal temperature (Fig. 10, dog 18) whereas temperature in the other comparably sized gingival melanoma was slightly higher than rectal (Fig. 10, dog 23). At the present time, we are unable to explain this temperature discrepancy. Possibly, sites where temperature is low are sites of poor tumor vascularity or tumor necrosis. An effect of thermocouple insertion on local or regional blood flow with resulting nonrepresentative temperature measurement cannot be discounted.

Temperature distribution in normal and tumor tissue in dogs undergoing whole body hyperthermia in the radiant heat device does not appear to be completely uniform. Exact reasons for the temperature distributions recorded in this project are not completely clear but possibly relate to differences in anatomic location of the tissue being measured, regional blood flow, metabolic heat production, and amount of adjacent insulating tissue. Temperature nonuniformity during whole body hyperthermia may affect the extent and distribution of hyperthermic cytotoxicity and hyperthermic chemo- or radiosensitization resulting from combination of whole body hyperthermia with radiotherapy or chemotherapy thereby influencing whether therapeutic gain will be achieved; also, toxicity patterns seen when whole body hyperthermia is combined with chemotherapy or radiotherapy are likely to be a direct function of the temperature nonuniformity present.

Finally, data reported herein were obtained from a limited number of sites in a limited number of dogs prompting the qualitative rather than statistical analysis. Nevertheless, information generated by these studies is of potential value relative to the use of whole body hyperthermia for cancer treatment. Data reported herein support the need for further investigation and characterization of temperature distributions during whole body hyperthermia and effects of invasive thermometry on such.

REFERENCES


Temperature Measurements in Normal and Tumor Tissue of Dogs Undergoing Whole Body Hyperthermia

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