Use of Insulation to Reduce Extremity Temperature Nonuniformity during Whole Body Hyperthermia in Dogs

Donald E. Thrall, Rodney L. Page, and Deborah A. McLeod

School of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina 27606

ABSTRACT

Previously we have shown in dogs that tibial bone marrow and s.c. tissue temperatures are lower than rectal temperature during the plateau phase of whole body hyperthermia with the use of a radiant heating device. In an attempt to increase thermal dose to these sites during whole body hyperthermia, we applied insulation to an extremity prior to the plateau phase of heating. We found that extremity insulation during whole body hyperthermia resulted in increased s.c. tissue and tibial bone marrow temperatures. With insulation, tibial bone marrow and rectal temperature were nearly equal but s.c. tissue temperature, although greater than without insulation, remained lower than rectal temperature. High efficiency extremity insulation or supplemental heating techniques may be necessary during whole body hyperthermia with the use of the radiant heat device in order to assure that extremities receive the prescribed thermal dose.

INTRODUCTION

Extensive temperature nonuniformity has been identified in normal and tumor tissue during local and regional hyperthermia (1, 2). Such temperature nonuniformity is disadvantageous as it could result in considerable variation in the dose modifying effect of hyperthermia on chemotherapy or radiotherapy. One potential advantage for use of whole body hyperthermia as opposed to local or regional hyperthermia is the possibility of more homogeneous tissue temperature distribution. This potential for more uniform heating may partially offset the maximum temperature limitation of 42°C associated with whole body hyperthermia.

Previously, we evaluated temperature in normal and tumor tissue of dogs undergoing whole body hyperthermia in a radiant heat device (3). We found that s.c. and tibial bone marrow temperatures were greater than rectal temperature during heating but fell below rectal temperature during plateau temperature conditions by as much as 1.3°C. The finding of decreased tibial bone marrow temperature during whole body hyperthermia has also been previously reported in pigs (4). These findings are significant relative to the reduced extent of hyperthermic cytotoxicity and radiosensitization or chemosensitization encountered in tissues where temperatures are lower than the targeted temperature of 42°C. Thus, areas such as s.c. tissues and tibial bone marrow may be sanctuaries for residual cancer because of insufficient heating.

It was the purpose of the experiments described herein to test the hypothesis that application of insulation to the extremities of dogs undergoing whole body hyperthermia reduces temperature nonuniformity.

MATERIALS AND METHODS

Tibial bone marrow and s.c. temperatures were measured in both pelvic limbs of 7 and 12 dogs, respectively, undergoing whole body hyperthermia in a radiant heat device (Enthermics Medical Systems, Inc., Menomonee Falls, WI). Specific details of the radiant heat device have been previously reported (3, 5, 6). Dogs in which tibial bone marrow temperature was measured were normal mongrel dogs, while dogs in which s.c. temperature was measured were pet dogs with cancer undergoing therapeutic whole body hyperthermia and chemotherapy. Simultaneous measurement of s.c. and tibial bone marrow temperature was not done.

For whole body hyperthermia, dogs were under general anesthesia as described previously (3, 7). Briefly, dogs were premedicated with atropine, Valium, and oxymorphone. Anesthesia was induced with thiopental and atracurium and maintained with positive pressure ventilation (fraction inspired × oxygen = 1.0, 16 breaths/min), continuous atracurium infusion, and i.v. bolus doses of thiopental and oxymorphone.

After anesthesia induction, dogs were inserted into the radiant heat device. One of two canine size devices was used for these studies. Both devices are hemiovoid in shape with open ends. The base diameter and center height of both devices are the same, approximately 56 and 84 cm, respectively. Heating elements in both devices are thermostatically controlled. One device has a length of approximately 43 cm, while the other device has a length of approximately 81 cm. In addition, the interior heating surface of the short device is uncoated polished metal, while the heating surface of the longer device was coated by the manufacturer with a black emulsion to increase emissivity. The open ends of the device are routinely covered with a heat reflective material during the heating period. The heat reflective material is usually raised when the rectal temperature reaches 41.8°C so that rectal temperature does not overshoot the targeted value of 42°C. Rectal temperature can be accurately controlled by adjustment of the position of the reflective material and thermostat settings.

Thermocouples were inserted into the tibial bone marrow and tibial s.c. tissues of both pelvic limbs as previously described (3). Rectal and air temperature were also measured as previously described (3). Air temperature was measured 1 cm above the abdominal skin. All thermometers were calibrated prior to each use. Once the dog was placed in the device, all temperatures were recorded every 5 min. Dogs were heated as previously described (3), with the exception that insulation material (goose down) was applied to one pelvic limb when the reflective material was raised to reopen the ends of the heat device, i.e., rectal temperature of 41.8°C. The target rectal temperature of 42°C was maintained for 60 min.

All measured temperatures were corrected based on calibration data. The difference between the corrected tibial bone marrow and corrected s.c. temperatures and the corrected rectal temperature were calculated for each time period. These derived variables are referred to as relative tibial bone marrow and relative s.c. temperatures. The difference between the mean relative tibial bone marrow (n = 7) and mean relative s.c. (n = 12) temperatures in insulated and uninsulated extremities was compared at each measurement time by using the paired t test. In addition, an analysis of variance procedure was performed in order to determine if the size of heating device influenced measured temperature values.

RESULTS

Plots of mean relative s.c. tissue and mean relative tibial bone marrow temperatures for insulated and uninsulated extremities as a function of heating time are shown in Figs. 1 and 2. Insulation results in a statistically significant increase in temperature at both sites during the later part of the plateau phase.
The arrow indicates the time at which one extremity was insulated. Temperatures in the insulated extremity are only slightly less than rectal temperature during the plateau phase. Times at which the mean values are statistically different are indicated by * (0.040 > P > 0.007). Bars, SE.

![Mean Tibial Marrow Temperature](image1)

**Fig. 1.** Mean insulated (△) and noninsulated (□) relative tibial bone marrow (site minus rectal) temperatures in 7 dogs undergoing whole body hyperthermia. The arrow indicates the time at which one extremity was insulated. Temperatures in the insulated extremity are only slightly less than rectal temperature during the plateau phase. Times at which the mean values are statistically different are indicated by * (0.040 > P > 0.007). Bars, SE.

![Mean Subcutaneous Temperature](image2)

**Fig. 2.** Mean insulated (△) and noninsulated (□) relative s.c. (site minus rectal) temperatures in 12 dogs undergoing whole body hyperthermia. The arrow indicates the time at which one extremity was insulated. Temperatures in the insulated extremity are only slightly less than rectal temperature during the plateau phase. Times at which the mean values are statistically different are indicated by * (0.022 > P > 0.007). Bars, SE.

of whole body hyperthermia. With insulation, tibial bone marrow temperature and rectal temperature were nearly equal, but s.c. tissues, although warmer than without insulation, remained cooler than rectal temperature.

Measured tibial bone marrow temperature was significantly different between short versus long heating devices at only one time (t = −25 min) during the heating phase (P = 0.033). Device size was not significantly related to measured s.c. temperature at any time. However, in reviewing absolute temperature values, there was a trend for temperatures measured in the short device to be higher during heating and cooler during the plateau phase than temperatures measured in the long device. The magnitude of this difference ranged from 0.1 to 0.7°C.

**DISCUSSION**

The initial finding that tibial bone marrow temperature in dogs undergoing whole body hyperthermia in a radiant heat device was higher than rectal temperature during heating but fell below rectal temperature during plateau conditions was unexpected. In those experiments, femoral bone marrow temperature was also measured and was found to behave differently. Femoral bone marrow temperature was lower than rectal temperature during heating but gradually equaled and slightly exceeded rectal temperature during the plateau phase. Thus, in noninsulated conditions, bone marrow temperature in dogs undergoing whole body hyperthermia in a radiant heat device seemingly depends on the anatomic location and morphology of the bone in which temperature was measured. The tibia, being a relatively small bone with little muscular covering, appears to behave as a superficial tissue, being warmer than rectal temperature during the heating phase. During the plateau phase of heating when skin temperature and temperature in the radiant heat device decrease, tibial bone marrow temperature falls below rectal temperature. Tibial bone marrow temperature also decreased more rapidly and to a lower absolute temperature during cooling than did femoral bone marrow, again supporting the similarity in behavior between tibial bone marrow and superficial tissues such as s.c. temperature (3). The cause for these fluctuations in tibial bone marrow temperature during whole body hyperthermia is unknown. Perhaps they result from countercurrent heat exchange between artery-vein pairs (8, 9). During heating, superficial blood would be warmer than rectal temperature and could result in additional heating of incoming arterial supply to tibial bone marrow by countercurrent heat exchange. Similarly, during the plateau phase, cool superficial blood could decrease the temperature of arterial supply to tibial bone marrow by the same mechanism. The femur being more centrally located within the thigh may be less affected by countercurrent heat exchange and its temperature would more closely parallel rectal temperature. Nevertheless, we chose to test the hypothesis that extremity insulation would be useful in maintaining s.c. tissue and tibial bone marrow temperature, as well as temperature in other small bones, at target temperature during the plateau phase.

We found that extremity insulation during the plateau phase of whole body hyperthermia is effective in reducing bone marrow and s.c. temperature nonuniformity. Insulation results in a statistically significant increase in tibial bone marrow temperature during the plateau phase, with tibial marrow temperature being essentially the same as rectal temperature (Fig. 1). Insulation also results in a statistically significant increase in s.c. temperature but s.c. temperature remains below the target temperature during the plateau phase (Fig. 2).

The fact that s.c. temperature was lower than tibial bone marrow temperature in insulated extremities suggests that the insulation used was incapable of preventing normal temperature gradients that probably exist in extremities under euthermic conditions from redeveloping (8, 9). Regardless of the cause, our data suggest that during whole body hyperthermia with the radiant heat device, insulation alone may not be adequate to maintain target temperature at s.c. limb sites. More efficient insulation or supplemental heating techniques may be necessary in such anatomic areas. Use of insulation may not be as critical for maintaining bone marrow temperature in bones surrounded by a large muscle mass, such as the femur, at the targeted value as the surrounding muscle seemingly acts as an insulator (3).

The relative size of the radiant heat device to the patient is a situation which deserves further investigation. Even though our data did not indicate a significant relationship between device size and measured temperature, P values relating device size and relative tibial bone marrow temperature during the heating
phases were commonly in the range $0.06 < P < 0.15$, suggesting that with a larger number of experimental animals device size might be significant. Tibial and s.c. temperatures measured in the noninsulated extremity in the short versus long device were subsequently compared at each time period. Even though there was no statistically significant difference, temperatures measured in the short device were consistently higher during heating and lower during the plateau phase than temperatures in the long device. The magnitude of this difference ranged from 0.1 to 0.7°C. These data suggest that temperature nonuniformity may be greater in situations where the size of the radiant heat device is small in relation to the patient. This topic deserves further investigation.

In summary, although extremity insulation is effective in reducing tissue temperature nonuniformity during whole body hyperthermia in the radiant heat device, complete extremity temperature uniformity was not achieved as s.c. tissue temperature remained below rectal temperature during the plateau phase. High efficiency extremity insulation or supplemental heating techniques may be necessary during whole body hyperthermia with the use of the radiant heat device in order to assure that extremities receive the prescribed thermal dose.

ACKNOWLEDGMENTS

The authors acknowledge the helpful assistance of Dr. Mark Dewhirst in discussion of these data.

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