Thermal and Physiologic Responses to 1200-MHz Radiofrequency Radiation: Differences between Exposure in E and H Orientation (43109)

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Abstract. **Ketamine-anesthetized Sprague-Dawley rats were exposed to far-field 1200-MHz continuous wave radiofrequency radiation in both E and H orientations (long axis of animal parallel to electric or magnetic field, respectively). Power densities were used that resulted in equivalent whole-body specific absorption rates of approximately 8 W/kg in both orientations (20 mW/cm² for E and 45 mW/cm² for H). Exposure was conducted to repeatedly increase colonic temperature from 38.5 to 39.5°C in both orientations in the same animal. Irradiation in E orientation resulted in greater colonic, tympanic, left subcutaneous (side toward antenna), and tail heating. The results indicated a more uniform distribution of heat than that which occurred in previous experiments of 2450-MHz irradiation in E and H orientation. A lack of significant differences in blood pressure and heart rate responses between exposures in the two orientations in this study suggest that greater peripheral heating, as was seen in the earlier study of 2450 MHz, is necessary for these differences to occur.** [P.S.E.B.M. 1990, Vol 194]

An increase in body temperature is a primary effect of exposure to high levels of radiofrequency radiation (RFR). Absorption of RFR is dependent upon irradiation frequency and orientation of the field relative to body dimensions (1, 2). Exposures to RFR of different carrier frequencies result in different rectal heating rates in rats (3) and rhesus monkeys (4); faster heating occurs during irradiation near the resonant frequency. Differences in whole-body average specific absorption rate (SAR) in rat carcasses irradiated at 2450 MHz in E versus H orientation (long axis of body parallel to electric or magnetic field, respectively) have been reported by Chou *et al.* (5), D'Andrea *et al.* (6), and McRee and Davis (7). Lotz (4) found that restrained rhesus monkeys exposed to 225-MHz RFR (near resonance) exhibited a greater increase in rectal temperature during E orientation exposure than during H orientation exposure.

In most recent studies of biologic effects of RFR, the amount of energy absorbed has been stated in terms of whole-body SAR. This value, however, does not provide complete information concerning the distribution of heat within the body. In studies of environmental heating, core to skin gradients are usually assumed to be minimal (8). During RFR exposures at relatively high frequencies, however, surface heating occurs more quickly than internal heating (9) and large thermal gradients exist within the animal.

Experiments by Frei *et al.* (10) and Jauchem *et al.* (11) revealed unequal heating patterns in anesthetized rats exposed to 2800- and 5600-MHz RFR. Subcutaneous and tympanic temperatures were greater than colonic temperature (T_c) at both frequencies. Frei *et al.* (12) observed that, in anesthetized rats exposed to 2450-MHz RFR, irradiation in E orientation resulted in greater peripheral and tympanic hearing, while irradiation in H orientation caused greater core heating. The differences in sites of energy deposition significantly affected the animals' physiologic responses to RFR.

Early studies of physiologic responses to RFR-induced hyperthermia revealed changes in heart rate (HR), blood pressure (BP) (13, 14), and respiration (15). The effects of thermal gradients resulting from RFR exposure at different frequencies and orientations

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on physiologic responses have not been completely elucidated. The purpose of the present study was to determine the effects of 1200-MHz irradiation in E and H orientation on patterns of heat deposition, HR, BP, and respiratory rate (RR) in anesthetized rats. Although behavioral responses of rats exposed to RFR of high peak power at frequencies of approximately 1200 MHz have been studied (16), cardiovascular and respiratory changes in rats exposed to this frequency have not been reported previously. This frequency approximates that of particular high-peak power stationary tracking radars for military applications and naval ship radars (17).

Materials and Methods

Animals and Physiologic Monitoring. Fifteen male Sprague-Dawley rats (Charles River Laboratories), weighing between 240 and 300 g (mean ± SE, 270 ± 4 g) were used in this study. Prior to experimentation, animals were housed in polycarbonate cages with free access to food and water and maintained on a 12-hr/12-hr light/dark cycle (lights on at 0600) in a climatically controlled environment (ambient temperature 24 ± 1°C).

Before surgery, animals were fasted 18 hr (water *ad libitum*). Ketamine HCl (Vetalar) was administered intramuscularly (150 mg/kg) for anesthesia, with supplemental doses provided as necessary during experimentation. Administration of ketamine at approximately this dose provides adequate anesthesia in Sprague-Dawley rats (18), and results in a stable animal preparation compatible with physiologic monitoring. A Teflon cannula was inserted into the left carotid artery to measure arterial blood pressure.

Immediately after surgery, the animal was placed on a holder in the RFR exposure chamber. The holder consisted of seven 0.5-cm (outside diameter) Plexiglas rods mounted in a semicircular pattern on 4- × 6-cm Plexiglas plates (0.5-cm thick). The animal was instrumented for continuous monitoring and recording of BP and RR, as described previously (11, 19). HR was determined from pulse-pressure recordings. Temperature was monitored at five sites: (i) colonic (5–6 cm post-anus), (ii) left subcutaneous (lateral, midthoracic, side facing the antenna), (iii) right subcutaneous (lateral, midthoracic, side away from RFR source), (iv) right tympanic, and (v) tail. The tip of the tail probe was inserted under the skin approximately 2 cm from the base of the tail. The non-RFR-perturbing thermistor probes were attached to a BSD-200 precision thermometry system (BSD Medical Corp.) to obtain continuous (12-sec sampling intervals) temperature readings.

RFR Equipment. The RFR fields were generated by a model 1326 RF power source (Cober Electronics, Inc.) and transmitted by a model 110 L standard-gain horn antenna (Struthers Electronic Corp.). Irradiation was performed under far-field conditions (animal positioned 170 cm from antenna) and the incident power density of the field was determined with an electromagnetic radiation monitor (model 8616, Narda Microwave Corp., employing a model 8626 probe). During exposures, generator power output was monitored continuously with a model 3128 power meter (Bird Electronic Corp.) and recorded on a Gould 2600S recorder. Irradiation was conducted in an Eccosorb RF-shielded anechoic chamber (Rantec, Emerson Electric Co.) at Brooks Air Force Base, Texas. The chamber temperature (27 ±0.5°C) and relative humidity (20 ± 5%) were monitored during experimentation.

Exposure Conditions. The experiments were designed to compare effects of RFR exposure at equivalent whole-body SAR in both orientations. The animals were exposed individually to 1200-MHz continuous-wave RFR at power densities of 20 and 45 mW/cm^2 in E and H orientation, respectively. These power densities resulted in whole-body average SAR of 8.0 ± 0.3 (mean ± SE) and 8.1 ± 0.4 W/kg. The SAR were determined calorimetrically according to the methods of Allen and Hurt (20) and Padilla and Bixby (21) in six rat carcasses for each orientation.

Since temperature increases during RFR exposure of live animals are not related solely to the absorption of RFR energy (22), we refer to live animal changes as specific heating rates (in W/kg), to be distinguished from the SAR in animal carcasses. The local specific heating rates and SAR were determined as explained previously (12).

The initial T_c before RFR exposure was 36.3 ± 0.2°C (mean ± SE). A stable regimen of T_c change was used for comparing the effects of irradiation in E and H orientation. The durations of RFR exposure to accomplish a 1°C T_c increase differed among animals; however, since this study focused on thermoregulatory processes, a consistent change in temperature was considered to be more important than a consistent duration of exposure. After initial exposure in E or H orientation had increased T_c to 39.5°C, irradiation was discontinued. When temperature returned to 38.5°C, irradiation was initiated until T_c again increased to 39.5°C. This procedure was repeated for three cycles. The antenna was then rotated and three additional cycles were completed in the second orientation. The repeated exposures were conducted to determine whether changes in HR, BP, and RR were consistent over the three cycles in each orientation. The orientation in which the animals were first exposed was alternated daily. After irradiation in both orientations, the animals were euthanized and the carcasses were exposed to RFR in E or H orientation for 12–15 min.

Statistical Analysis. Student's *t* test for paired data (two-tailed) was used to determine whether there were significant differences in T_c rise time, T_c recovery time, and levels of subcutaneous, tympanic, and tail temper-

ature increase between the two orientations. Student's *t* test for unpaired data was used to determine whether there were significant differences between the rates of temperature change in the carcasses irradiated in the two orientations, and between the rates in carcasses and live animals. Analysis of variance with two groups (based on order of exposure to the two orientations; i.e., E first versus H first) with repeated measurements of cycles, orientation, and temperature was applied to determine whether there were significant changes in HR, BP, and RR during the 1°C change in T_c. *P* values of less than 0.05 were considered to indicate significance in all tests.

Table I. Rise Time and Recovery Time for a 1°C Colonic Temperature Change in Rats ($n = 15$) Exposed in E and H Orientation to 1200-MHz Radiofrequency Radiation (SAR, 8 W/kg)

Exposure condition	Rise time (min)	Recovery time (min)
E Orientation	8.9 ± 0.6[a]	13.1 ± 1.5[a]
	—[b]	
H Orientation	10.2 ± 0.8	11.9 ± 1.4

[a] Mean ± SE.
[b] Significant difference between results in E versus H orientation ($P < 0.05$).

Table II. Local Temperature Increase (Mean ± SE) Accompanying a 1°C Colonic Temperature Increase in Rats ($n = 15$) Exposed to 1200-MHz RFR in E and H Orientation (SAR, 8 W/kg)

Temperature monitoring site	Temperature increase (°C)	
	E Orientation	H Orientation
Left subcutaneous	1.5 ± 0.1[a]	0.4 ± 0.04[a]
Right subcutaneous	0.6 ± 0.1[a]	0.7 ± 0.1[a]
Tympanic	0.9 ± 0.04[a]	0.7 ± 0.1[a]
Tail	5.5 ± 0.3[a]	2.0 ± 0.2[a]

[a] Significant difference between results in E versus H orientation ($P < 0.05$).

Table III. Local Specific Heating Rates (Mean ± SE) in Rats ($n = 15$) Exposed to 1200-MHz RFR in E and H Orientation (SAR, 8 W/kg)

Temperature monitoring site	Specific heating rate (W/kg ± SEM)	
	E Orientation	H Orientation
Left subcutaneous	18 ± 1[a]	5 ± 1[a]
Right subcutaneous	7 ± 0.3[a]	8 ± 0.2[a]
Colonic	12 ± 1	12 ± 1
Tympanic	11 ± 0.3[a]	8 ± 0.2[a]
Tail	78 ± 2[a]	27 ± 2[a]

[a] Significant difference between results in E versus H orientation ($P < 0.05$).

Table IV. Local Specific Absorption Rates (Mean ± SE) in Rat Carcasses ($n = 12$) Exposed to 1200-MHz RFR in E or H Orientation (SAR, 8 W/kg)

Temperature monitoring site	Specific absorption rates (W/kg ± SEM)	
	E Orientation	H Orientation
Left subcutaneous	22 ± 1[a]	4 ± 0.4[a]
Right subcutaneous	5 ± 1[a]	8 ± 0.4[a]
Colonic	12 ± 1	13 ± 2
Tympanic	13 ± 1[a]	9 ± 1[a]
Tail	80 ± 3[a]	35 ± 3[a]

[a] Significant difference between results in E versus H orientation ($P < 0.05$).

Table V. Cardiovascular and Respiratory Changes (Mean ± SE) in Rats Exposed to 1200-MHz RFR in E and H Orientation[a]

Parameter and orientation	Colonic temperature (°C)			
	38.5	39.0	39.5	39.0
Heart rate (beats/min)				
E	299 ± 9	306 ± 9	318 ± 10	306 ± 10
H	287 ± 8	293 ± 8	299 ± 9	294 ± 8
Blood pressure (mm Hg)				
E	98 ± 3	102 ± 2	105 ± 2	96 ± 3
H	94 ± 3	96 ± 3	97 ± 3	93 ± 3
Respiratory rate (breaths/min)				
E	104 ± 6	108 ± 5	113 ± 7	101 ± 6
H	109 ± 7	110 ± 8	116 ± 7	107 ± 7

[a] Rats ($n = 15$) were irradiated (SAR, 8 W/kg) to change colonic temperature from 38.5 to 39.5°C, after which irradiation was stopped and temperature allowed to return to 38.5°C.

Results

Data obtained from repeated cycles in the two exposure orientations were averaged for each animal and are expressed as group mean ± SE. Summarized in Table I are the times required for T_c to increase from 38.5 to 39.5°C during irradiation in E and H orientation, and to return to 38.5°C. The time to accomplish a 1°C T_c increase was significantly longer in H than in E orientation; the time required for T_c to recover to 38.5°C was not significantly different. Shown in Table II are the left and right subcutaneous, tympanic, and tail temperature increases that accompanied the 1°C T_c increase. Tail temperatures at the beginning of the cycles were 31.7 ± 0.6°C and 32.0 ± 0.5°C in E and H orientation, respectively. Initial temperatures at the other sites were in the same range as T_c. The left subcutaneous, tympanic, and tail temperature increases were significantly greater in E than in H orientation; the right subcutaneous temperature change, however, was significantly less in E than in H orientation. Local specific heating rates, determined as described previ-

ously (12), are displayed in Table III. The local SAR obtained during carcass irradiation are shown in Table IV. The same pattern of heating occurred in both live animals and carcasses. In both cases, the left subcutaneous, tympanic, and tail temperature changes were significantly greater in E than in H orientation. There were no significant differences between specific heating rates (live animals) and SAR (dead animals).

Presented in Table V are the BP, HR, and RR changes that accompanied the 1°C T_c cycles. HR ($F = 38.46$, $P < 0.0001$), BP ($F = 9.24$, $P < 0.0001$), and RR ($F = 9.46$, $P < 0.0001$) each varied significantly with temperature ($df = 3, 39$ in each case). There were no interactions between temperature and the other factors. F values for interaction of temperature with order of exposure to the two orientations ($df = 3, 39$) were 1.44, 0.96, and 0.27 for HR, BP, and RR, respectively. F values for interaction of temperature with cycles ($df = 6, 78$) were 1.34, 0.49, and 1.22. F values for interaction of temperature with orientation ($df = 3, 39$) were 1.68, 1.47, and 0.41. In all cases, values returned to near baseline levels during recovery periods. Separate responses for E and H orientations are presented in Table V.

Discussion

The present experiments were conducted using anesthetized rats. It should be emphasized that, in unanesthetized animals, the rate of temperature increase, and the changes in HR, BP, and RR could be different. This issue has been addressed in a previous report (23).

In the previous study of 2450-MHz RFR exposure (12), average whole-body SAR was approximately 14 W/kg. In the present experiments, due to limitations of the RF power source, the maximum average whole-body SAR that could be achieved in H orientation was approximately 8 W/kg. Although the present experiments were not designed to make direct statistical comparisons with results of the previous 2450-MHz series, qualitative differences or similarities may be noted.

Heat Distribution. Several significant differences that occurred between results in E versus H orientation in these 1200-MHz experiments are consistent with a previous study of 2450-MHz exposure (12): the increases in left subcutaneous and tympanic temperatures were greater in E orientation, while the right subcutaneous temperature increase was greater in H orientation at both frequencies. The magnitude of the differences between results in E versus H orientation, however, was lower in the present experiments than in the study of 2450-MHz exposure.

A major difference between the results of 1200-MHz irradiation and the previous results of exposure to 2450-MHz RFR was seen in the T_c responses. At 2450 MHz, T_c increased faster in H orientation, while at 1200 MHz, T_c increased faster in E orientation. Despite different SAR used at the two frequencies, the times required for T_c to increase 1°C were similar. This can be explained by the frequency difference; the lower frequency is nearer to the resonant frequency for rats of this size. Maximum energy absorption in medium-sized rats occurs at approximately 600–700 MHz (2, 6).

Heart Rate and Blood Pressure. The HR and mean arterial BP increases during RFR exposure in the present experiments are generally consistent with earlier results obtained at 2450 MHz (12). In the 2450-MHz series, the increases were significantly greater in E than in H orientation. In the present study, however, there were only trends toward greater HR and BP increases in E than in H orientation; the changes were not significantly different. Possibly, the greater subcutaneous temperature (on the left side) that occurred during E orientation exposure at 2450-MHz caused greater changes in HR and BP. Changes in skin temperature can exert a strong influence on HR (24, 25). In the present experiments, the increase in left subcutaneous temperature was almost four times as great in E as in H orientation. This may explain, in part, the slightly greater increase in HR during E orientation exposure.

Many reports have indicated that the *rate* of temperature increase, rather than simply the absolute temperature change, plays an important role in thermoregulation (26–29). Earlier studies of rats exposed to 5600- (11) and 2800-MHz RFR (10) showed that increases in HR were related to the rate of temperature change. In the present experiments, the rates of temperature increases at most sites measured were significantly faster in E than in H orientation exposure. This difference in rate of temperature change may partially explain the greater increase in HR that occurred during E orientation irradiation.

Respiratory Rate. Exposure to RFR can cause increased RR in animals (14, 15). As Gordon and Long (30) have pointed out, compared with other physiologic or behavioral responses, threshold levels of RFR-induced heating required to effect an increase in RR are relatively high. These authors found that during 2450-MHz RFR exposure at an ambient temperature of 30°C, hamsters and mice exhibited increases in RR at SAR of 2 and 10 W/kg, respectively. At higher SAR, RR continued to increase linearly.

In previous studies, ketamine-anesthetized rats exposed to 2800- (10, 31, 32) and 5600-MHz RFR (11, 33) at SAR ranging from 6 to 21 W/kg exhibited no significant changes in RR during a 1°C change in T_c (from 38.5 to 39.5°C). (Ketamine, unlike other general anesthetics, does not cause respiratory depression [34].) The above exposures were conducted with the animals in H orientation. Possibly, the change in body temperature was below the threshold necessary to result in

increased RR. Earlier work by Saxton (35) showed that human subjects exhibited increased RR only when body temperature changed by at least 1.5°C. In another study dealing with terminal exposure of anesthetized rats, changes in RR were noted, but only when the colonic temperature exceeded 41–41.5°C (36). In a recent study, Frei *et al.* (12) found that during 2450-MHz irradiation in the H orientation (but not E orientation), RR significantly increased in rats when colonic temperature changed from 38.5 to 39.5°C. In the present study of 1200-MHz exposure, RR increased significantly; there was no significant difference in the RR increase between E and H orientation. On the basis of these findings, it is possible that deposition of RFR energy deeper into the core, which occurs at the lower frequencies, is necessary for an increase in RR. The importance of activation of deep thermal receptors in stimulation of respiration has been postulated previously (37, 38).

Tail Temperature. The tail plays an important role in heat dissipation in the rat (39). Rand *et al.* (40) reported that as much as 20% of the total heat production in the rat could be lost from the tail. Evidence suggested that increased heat loss was associated with increased total blood flow to the tail. Young and Dawson (41) found that tail vasodilation occurred abruptly and was an all or none phenomenon. Other investigators have shown that vasodilation of the tail of the unanesthetized rat does not occur until core temperature reaches at least 39.0°C (42). Grant (43), however, reported that the threshold for vasodilation in the pentobarbital-anesthetized rat was approximately 37°C. Since regional blood flow in the ketamine-anesthetized rat has been reported to be similar to that in the unanesthetized rat (44), it is possible that, in the present study, cycling T_c between 38.5 and 39.5°C could have caused the tail to respond to the heat load by vasodilation.

To summarize the present study, 1200-MHz irradiation in E orientation resulted in greater heating than in H orientation at most sites where temperature was measured. In both E and H orientations, the distribution of heat throughout the body was more uniform than during previous experiments of 2450-MHz irradiation. The differences between results during E versus H orientation, at equivalent average whole-body SAR, were less in the present 1200-MHz series than the previous 2450-MHz series. Comparison of temperature distribution and cardiovascular responses at the two frequencies suggests that the smaller HR and BP changes at the lower frequency may have been related to the lower peripheral temperature change during irradiation.

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19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Ketamine-anesthetized Sprague-Dawley rats were exposed to far-field 1200-MHz continuous wave radiofrequency radiation in both E and H orientations (long axis of animal parallel to electric or magnetic field, respectively). Power densities were used that resulted in equivalent whole-body specific absorption rates of approximately 8 W/kg in both orientations (20 mW/cm^2 for E and 45mW/cm^2 for H). Exposure was conducted to repeatedly increase colonic temperature from 38.5 to 39.5°C in both orientations in the same animal. Irradiation in E orientation resulted in greater colonic, tympanic, left subcutaneous (side toward antenna), and tail heating. The results indicated a more uniform distribution of heat than that which occurred in previous experiments of 2450-MHz irradiation in E and H orientation. A lack of significant differences in blood pressure and heart rate responses between exposures in the two orientations in this study suggest that greater peripheral heating, as was seen in the earlier study of 2450 MHz, is necessary for these differences to occur.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	Unclassified

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