Effect of Cell Phone Radiofrequency Radiation on Body Temperature in Rodents: Pilot Studies of the National Toxicology Program’s Reverberation Chamber Exposure System

Michael E. Wyde,1* Thomas L. Horn,2 Myles H. Capstick,3 John M. Ladbury,4 Galen Koepke,4 Perry F. Wilson,4 Grace E. Kissling,1 Matthew D. Stout,1 Niels Kuster,3 Ronald L. Melnick,1 James Gauger,2 John R. Bucher,1 and David L. McCormick2

1National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina
2IIT Research Institute, Chicago, Illinois
3IT’IS Foundation, Zurich, Switzerland
4National Institute of Standards and Technology, Boulder, Colorado

Radiofrequency radiation (RFR) causes heating, which can lead to detrimental biological effects. To characterize the effects of RFR exposure on body temperature in relation to animal size and pregnancy, a series of short-term toxicity studies was conducted in a unique RFR exposure system. Young and old B6C3F1 mice and young, old, and pregnant Harlan Sprague-Dawley rats were exposed to Global System for Mobile Communication (GSM) or Code Division Multiple Access (CDMA) RFR (rats = 900 MHz, mice = 1,900 MHz) at specific absorption rates (SARs) up to 12 W/kg for approximately 9 h a day for 5 days. In general, fewer and less severe increases in body temperature were observed in young than in older rats. SAR-dependent increases in subcutaneous body temperatures were observed at exposures ≥6 W/kg in both modulations. Exposures of ≥10 W/kg GSM or CDMA RFR induced excessive increases in body temperature, leading to mortality. There was also a significant increase in the number of resorptions in pregnant rats at 12 W/kg GSM RFR. In mice, only sporadic increases in body temperature were observed regardless of sex or age when exposed to GSM or CDMA RFR up to 12 W/kg. These results identified SARs at which measurable RFR-mediated thermal effects occur, and were used in the selection of exposures for subsequent toxicology and carcinogenicity studies. Bioelectromagnetics. 39:190–199, 2018. © 2018 The Authors. Bioelectromagnetics Published by Wiley Periodicals, Inc.

Keywords: wireless communication; rodents; body temperature; pregnancy; microwaves

INTRODUCTION

Since the first commercial cell phone systems were launched in the United States in 1983, usage has expanded steadily. In the United States, the wireless industry had more than an estimated 390 million subscribers in 2016 [Cellular Telecommunications Industry Association (CTIA), 2017]. According to a Pew Research Center Survey [2013], cell phones were being used by 91 percent of American adults. Given the extremely large number of people who use wireless communication devices, even a very small increase in the incidence of disease resulting from exposure to the radiofrequency radiation (RFR) generated by those devices could have broad implications for public health.

Cell phones and other commonly used wireless communication devices transmit information via
RFR. At high exposure levels, non-ionizing RFR can produce local thermal effects (tissue heating) that can damage temperature-sensitive biological structures and processes. Given the proximity of cell phone use to the head, there have been specific concerns raised about the possibility that RFR exposure from wireless devices can lead to increased risk of brain cancer. Although the levels of RFR generated by cellular telephones are modest, it is not currently known whether chronic exposure to low-level RFR, not resulting in measurable thermal effects, could impact human health. Therefore, potential increases in the risks of cancer, cognitive dysfunction, and other adverse health outcomes remain a public concern.

Studies investigating the carcinogenicity of RFR in rodents have not demonstrated a convincing association between RFR and increased incidences of tumors [Lin, 2017]. However, the value of many of these studies is limited by design features that reduce their utility to adequately assess the carcinogenicity of RFR. For example, several studies were conducted with a “Ferris wheel”-type RFR exposure system that requires animals to be restrained during exposure periods [Anderson et al., 2004; Smith et al., 2007; Tillmann et al., 2007]. To avoid stress in the restrained animals, these studies limited exposure to RFR to only 2 h per day. In chronic studies in Sprague–Dawley rats conducted by Chou et al. [1992] and Bartsch et al. [2010], the highest level of exposure, 0.4 Watts/kilogram (W/kg) and 0.13 W/kg, respectively, were at least an order of magnitude below exposures in other studies that exhibited no measure of toxicity [Smith et al., 2007; Tillmann et al., 2007], and were inadequate to assess chronic toxicity and carcinogenicity. In other studies, RFR exposures were based on time-averaged specific absorption rate (SAR) in the brain rather than in the whole body [La Regina et al., 2003; Anderson et al., 2004]. This approach is useful to evaluate the brain as the sole target tissue of interest, but is inadequate for addressing the overall carcinogenicity of RFR exposure in all tissues.

Additional studies of the effect of RFR on tumorigenesis in tumor-prone models, including Ptc1+/− knockout mice (brain tumors), Eμ-Pim1 transgenic mice (lymphomas), AKR mice (lymphomas and other hematopoietic neoplasms), and C3H mice (mammary tumors) have yielded conflicting results [Repacholi et al., 1997; Toler et al., 1997; Frei et al., 1998a,b; Utteridge et al., 2002; Sommer et al., 2004, 2007; Oberto et al., 2007; Saran et al., 2007; Lee et al., 2011]. Furthermore, the value of several of these studies in assessing carcinogenicity of RFR is also reduced by limitations in study design and/or RFR exposures.

To address the identified limitations, it was essential that additional rodent carcinogenicity studies be designed and performed using: (a) expanded study designs with greater statistical power; (b) increased durations of daily RFR exposure; (c) higher but still non-thermal levels of RFR exposure; (d) improved exposure and monitoring systems; and (e) detailed dosimetry models on which precise estimates of RFR exposure in specific organs could be characterized.

To address these goals, a collaboration between scientists at the National Institute of Environmental Health Sciences (NIEHS) and engineers at the National Institute of Standards and Technology (NIST) was established to design and evaluate the feasibility of an exposure system based on a reverberation chamber design. The reverberation chamber is a shielded room containing one or more excitation antennas with rotating horizontal and vertical paddles to ensure even distribution of statistically homogeneous RF fields within the chamber. This resolves the key limitations identified in previous studies by permitting whole-body exposures in unrestrained, individually-housed animals, and accommodating longer daily exposures. Large capacity reverberation chambers also support substantial increases in experimental group size. Because all animals are housed within an exposure volume of homogenous RFR, exposures can be carefully monitored and controlled, and precise dosimetric calculations can be performed. The feasibility of this approach was first demonstrated in a study performed at NIST in a standard reverberation chamber.

Based on these results, the Foundation for Research on Information Technologies in Society (ITIS; Switzerland) designed, developed, and built a prototype reverberation system that provided uniform, well-defined lifetime exposure to rats and mice that simulated exposure to mobile phone users. An RFR exposure facility consisting of reverberation chambers including RFR generation and monitoring systems was then constructed to expose rats and mice to 900 or 1,900 MHz, respectively, Code Division Multiple Access (CDMA) or Global System for Mobile Communication (GSM) modulated cell phone radiofrequency (RF) radiation, and installed at IIT Research Institute (ITRI; Chicago, IL). The RFR exposure system and animal exposure dosimetry are described in detail in Capstick et al. [2017] and Gong et al. [2016, 2017]. The design of the facility maximized suitability for toxicity/carcinogenicity studies including considerations of workflow and personnel health and safety, long-term housing of animals, and Good

Bioelectromagnetics
Laboratory Practice (GLP) compliance of hardware, software, and data. The overall system performance, the suitability of approaches used for signal generation, amplification and exposure monitoring, and temporal and spatial homogeneity of experimentally generated RF fields were evaluated by engineers from NIST.

Robust toxicology and carcinogenicity studies depend on the appropriate selection of RFR exposure levels. Exposure levels of RFR are generally quantified as a specific absorption rate (SAR), which is a measure of RF energy (in watts) absorbed by a unit of mass (in kg). While exposure to high SARs are known to induce acute toxicity through tissue heating, extended exposure to lower SARs may also lead to the disruption of thermoregulation by unknown mechanisms or simply through aging. Additionally, animal mass is a critical variable in RFR studies. Maintenance of a constant whole-body SAR for exposure requires increased RFR power as young animals age and grow larger. The current series of studies investigated the effect of RFR on body temperature and overt toxicity in young and aged B6C3F1 mice and young, aged, and pregnant Harlan Sprague–Dawley rats.

MATERIALS AND METHODS

Prior to the initiation of in vivo studies, study protocols were reviewed and approved by the IITRI Animal Care and Use Committee. All procedures involving animals were performed in compliance with U.S. Public Health Service policy on humane care and use of laboratory animals and the Guide for the Care and Use of Laboratory Animals [National Research Council, 1996].

RFR Exposures

A complete description of the design and function of the RFR reverberation chamber exposure system and the facility at IITRI is provided in detail in Capstick et al. [2017].

The facility consisted of identically-sized walk-in reverberation chambers (exterior dimensions \( 3.7 \times 2.2 \times 2.6 \) m). Individual chambers were equipped to expose a single group of individually-housed rats or mice to modulated (CDMA or GSM) RFR at a specific whole-body exposure level. To achieve target field strengths, the total RF power introduced into a given chamber was adjusted to the total mass of the animals (number of animals \( \times \) mean body weight). To maintain constant exposure levels (W/kg) in a given chamber, the electric field strengths (V/m) were regularly adjusted to reflect changes in the body weights of the exposed animals. Since adult male and female rats differ significantly in mass, male and female rats were exposed in separate chambers. Since there is very little sex-related difference in body mass in mice, male and female mice were individually housed in cages that were exposed in the same chambers. Control animals were housed in a chamber identical to the exposed animals, except without an active RFR antenna. Continuous monitoring of experimentally generated RF fields was performed via measurements generated by two independent sensors installed in each chamber [Capstick et al., 2017].

Animals and Husbandry

B6C3F1/N mice (Taconic, Germantown, NY) were received at approximately 3–4 weeks of age and were held in quarantine for a minimum of one week. Young mice were approximately 5 weeks old at the start of RFR exposures. For studies in aged mice, B6C3F1/N mice (Taconic) were received at approximately 7 weeks of age and held in quarantine for approximately 17 months. Aged mice were approximately 19 months of age at the start of RFR exposures. Sprague–Dawley rats (Harlan Laboratories, Indianapolis, IN) were received at 3–4 weeks of age and were held in quarantine for a minimum of one week. Young rats were approximately 5–7 weeks of age at the start of the exposures. Aged rats were approximately 21–22 weeks old (in the CDMA studies) or 9 months old (in the GSM studies) at the start of the exposures. Pregnant rats (approximately 12–14 weeks of age) were received on gestation day (GD) 3 or 4 and exposed from GD 10 to GD 15 (or GD 11 to GD 16, Cohort I, GSM only). Weights of the animals at study start are given in Table 1. All animals were held in quarantine until the start of the studies, and randomized and identified by tail tattoo. Throughout the study, animals were housed

| TABLE 1. Average Body Weight (g) at Study Start |
|-----------------------------------------------|
| GA M  | CDMA |
| Young mice |
| M     | 21   | 22   |
| F     | 19   | 18   |
| Aged mice |
| M     | 52   | 50   |
| F     | 57   | 54   |
| Young rats |
| M     | 157  | 158  |
| F     | 122  | 120  |
| Aged rats |
| M     | 504  | 470  |
| F     | 298  | 261  |
| Pregnant rats |
| F     | 248  | 253  |
individually on certified, irradiated hardwood bedding (P. J. Murphy Forest Products, Montvale, NJ) in polycarbonate solid bottom cages. Cages, feed, and bedding were changed at least once per week. Cages (23.5 cm L × 26.0 cm W × 21.0 cm H for rats and 23.5 cm L × 15.2 cm W × 15.6 cm H for mice) were housed in custom-designed fiberglass cage racks located within the reverberation chambers. Environmental conditions were controlled and monitored electronically. Each chamber was maintained on a 12 h light/dark cycle, with a temperature range of 20.6 to 23.9 °C and a humidity range of 50 ± 15% and 10 air changes per h. Young and aged rats and mice received certified NIH-07 feed and pregnant rats received certified NTP-2000 feed and pregnant rats received certified NIH-07 feed (Ziegler Brothers, Gardners, PA). City of Chicago tap water was provided to all cages via the facility-dedicated recirculating, reverse osmosis automatic watering system with ultraviolet purification technology (SE Lab Group, Cincinnati, OH). Animals had ad libitum access to food and drinking water throughout the quarantine and exposure periods. Food and water consumption were not measured during the studies. All animals were euthanized via 100% CO2 inhalation.

Study Design

Groups of mice or rats (n = 5/sex/group) were exposed to either GSM or CDMA RFR (rats = 900 MHz, mice = 1,900 MHz) at time-averaged SAR levels of 0, 4, 6, 8, 10, or 12 W/kg for 5 consecutive days. Since the exposure facility was capable of accommodating 3 exposure groups and a control group, exposures occurred in two cohorts. The first cohort was exposed at levels of 0, 4, 6, and 8 W/kg; the second included 0, 10, and 12 W/kg exposures. The same set of control animals was used in both cohorts. Daily exposures occurred over a period of 18 h and 20 min (11 AM to 2 PM CST; 3:40 PM to 7 AM CST with the system off from 7 to 11 AM and 2 to 3:40 PM) with continuous cycling of 10 min on and 10 min off. During each 10-min period, one modulation was active while the other was off. As a result, during each 24-h day, actual exposure to each modulation was for 9 h and 10 min. Staff observed animals and performed husbandry activities during the period of non-exposure. Examinations for mortality and moribundity and cage-side clinical observations were performed and recorded twice daily, at least 6 h apart. Formal (outside of cage) clinical observations were performed at randomization and daily on Days 2 to 6. Animals were weighed at randomization, prior to the initiation of exposure (Day 0), and after completion of the exposure (Day 6).

Body temperatures were measured via interscapular, subcutaneously-implanted temperature microchips and readers (Bio Medic Data Systems, Seaford, DE). Subcutaneous body temperatures were measured within approximately 1–2 min of the end of exposures (during the 10 min off exposure period) on Days 1, 3, and 5 at 1, 5, 20, 49, 53, 68, 97, 101, and 116 h after initiation of exposures. All studies were begun at 11 AM (CST). Additionally, body temperatures were measured at the end of an extended period of non-exposure during daily husbandry activities on Days 2 and 4. These measurements were recorded 3–3 h and 30 min after the end of exposures and 30–60 min prior to resuming exposures (approximately 23 and 71 h following initiation of the Day 1 exposures, respectively).

For pregnant rats, following the completion of exposure, Cohort II animals were held until GD 20. At that time they underwent Cesarean section to assess pregnancy status and determination of live and dead pups and resorptions. The weight of each live pup was measured, and the number of corpora lutea in the ovaries was counted.

Statistical Analysis

Body temperatures and Cesarean section data were analyzed using ANOVA followed by post hoc comparisons using Dunnett’s test (Systat Software, Chicago, IL); a minimum significance level of P < 0.05 was applied.

RESULTS

To determine the effect of RFR exposure on body temperature, the data from these studies were collected and evaluated by several methods. For the overall effect of increasing levels of RFR on body temperature, all temperature measurements that were collected immediately after cessation of exposure on Days 1, 3, and 5 for each exposure group were averaged (for all time points combined) and compared to non-RFR controls (data presented in Figs. 1–5). Data from the individual time points were also evaluated and compared to time-matched controls for each time point (data presented in Supplemental Tables S1–S14). Body temperature measurements were also recorded after a recovery period, ~3 h after cessation of the exposures on Days 2 and 4 of the study.

Body Temperature Following Exposure

Young rats. All young male and female rats exposed to all power levels of GSM or CDMA (900 MHz) RFR survived to the end of the studies. In young male rats exposed to GSM RFR, mean body temperatures were significantly higher in the groups exposed to ≥8 W/kg compared to controls (Fig. 1A and Supplemental
Table S1). Overall, mean body temperatures were elevated at more individual time points with increasing SAR compared to time-matched controls.

In young female rats exposed to GSM RFR, there were no significant changes in mean body temperatures (Fig. 1B). However, at some time points mean body temperatures were significantly higher than time-matched controls (Supplemental Table S1). These increases occasionally exceeded the time-matched control group by ≥1°C.

In young male rats exposed to CDMA RFR, mean body temperatures were significantly higher in the groups exposed to ≥10 W/kg (Fig. 1C and Supplemental Table S2). At 12 W/kg, most of the observed increases exceeded the time-matched control group by ≥1°C. At 10 W/kg, increases exceeded the time-matched control group by ≥1°C at 68 and 116 h.

In young female rats exposed to CDMA RFR, mean body temperatures were significantly higher only in the 8 W/kg group (Fig. 1D), and again, at some individual time points, significantly higher body temperatures were observed (Supplemental Table S2). Four of these five increases exceeded time-matched controls by ≥1°C. At 10 W/kg, body temperatures were significantly higher (but ≤1°C) at only 2 of the 9 time points. Unexpectedly, there were no exposure-related differences in body temperature at 12 W/kg.

**Aged rats.** All aged male rats exposed to 10 or 12 W/kg GSM RFR died during the first day of exposures. In aged male rats exposed to GSM RFR, mean body temperatures were significantly higher at 6 or 8 W/kg compared to controls (Fig. 2A and Supplemental Table S3). In aged females exposed to GSM RFR, exposures to 12 W/kg were discontinued at 20 h due to excessive increases in body temperature (>3°C). Mean body temperatures were significantly higher in the aged females exposed to ≥6 W/kg (Fig. 2B and Supplemental Table S3).

All aged male rats exposed to CDMA RFR at 12 W/kg died during the first day of exposure, and RFR exposures in aged male rats exposed to 10 W/kg CDMA RFR were discontinued on Day 1 due to increases in body temperature (>3°C). Mean body temperatures were significantly higher in the groups exposed to 6 or 8 W/kg compared to controls (Fig. 2C and Supplemental Table S4).
Although no mortality or clinical signs were seen in aged female rats exposed to CDMA RFR, mean body temperatures were significantly higher in the groups exposed to ≥6 W/kg (Fig. 2D and Supplemental Table S4). Mean body temperatures exceeded 1.0 °C compared to time-matched controls at most of the time points in 8, 10, and 12 W/kg aged females.

**Pregnant rats.** There was no effect of exposure on survival in any of the groups of pregnant rats exposed to GSM RFR for 5 days beginning on GD 6. Mean body temperatures were significantly higher in the groups exposed to ≥6 W/kg GSM RFR (Fig. 3A and Supplemental Table S5). The increases observed at all time points in the 12 W/kg GSM RFR group exceeded the time-matched controls by ≥1 °C.

There was no effect of exposure on survival in any of the groups of pregnant rats exposed to CDMA RFR for 5 days beginning on GD 6. Mean body temperatures were significantly higher in the groups exposed to ≥6 W/kg (Fig. 3B and Supplemental Table S6). All of the increases observed in the 12 W/kg females, and all but two significant increases in the 10 W/kg group, exceeded time-matched controls by ≥1 °C.

Dams from the 10 W/kg, 12 W/kg, and control group were evaluated by Cesarean section for potential effects of exposure on pregnancy. In the GSM RFR (900 MHz) exposed pregnant females, there were no differences in the number of live fetuses, but ammonium sulfide staining of the uterus identified a small increase in the number of resorption sites (mean 1.6 vs. 0), which reached statistical significance in the 12 W/kg group. There were no treatment-related effects on the number of live/dead pups, number of corpora lutea, or mean fetal weight (data not shown). In pregnant rats exposed to 10 or 12 W/kg CDMA RFR (900 MHz), no exposure-related findings were observed in the number of resorptions, number of corpora lutea, number of implantation sites, number of live and dead fetuses, or mean fetal weight.

**Young mice.** All young male and female mice exposed to all power levels of GSM or CDMA survived to the end of the studies. In young male mice exposed to GSM RFR, mean body temperatures were significantly higher in the group exposed to 12 W/kg (Fig. 4A and Supplemental Table S7). In young male mice exposed to CDMA RFR, mean body temperatures were significantly higher in the groups exposed to ≥6 W/kg (Fig. 4B and Supplemental Table S8).
temperatures were significantly higher only in the group exposed to 10 W/kg (Fig. 4C and Supplemental Table S8). No significant changes were observed in female mice exposed to GSM (Fig. 4B and Supplemental Table S7) or CDMA (Fig. 4D and Supplemental Table S8) RFR.

**Aged mice.** All aged male and female mice exposed to all power levels of GSM or CDMA survived to the end of the studies. No significant differences in mean body temperature were observed between aged male mice exposed to RFR regardless of GSM or CDMA modulation (Figs. 5A and 5C and Supplemental Tables S9 and S10). There were also no significant differences in mean body temperature in aged female mice exposed to GSM RFR (Fig. 5B and Supplemental Table S9). In aged female mice exposed to CDMA RFR, mean body temperatures were significantly higher in the group exposed to 8 W/kg (Fig. 5D and Supplemental Table S10).

---

**Fig. 3.** Average body temperatures of pregnant female rats after 5 days of exposure up to 12 W/kg GSM or CDMA RFR. Studies were conducted in two cohorts, differentiated by symbols as follows: ● Control, 4, 6, 8 W/kg; ○ Control, 10, 12 W/kg. *P < 0.05.

**Fig. 4.** Average body temperatures of young male and female mice after 5 days of exposure up to 12 W/kg GSM or CDMA RFR. Studies were conducted in two cohorts, differentiated by symbols as follows: ● Control, 4, 6, 8 W/kg; ○ Control, 10, 12 W/kg. *P < 0.05.
Body Temperature Following RFR Exposure
Recovery Period

In addition to body temperatures measured within 1–2 min of cessation of RFR exposure, body temperature measurements were also recorded on Days 2 and 4 after a recovery period of 3 h to 3 h and 30 min.

As a result of decreased survival and termination of excessive exposures in aged rats, no body temperature data were obtained on Days 2 or 4 for males exposed to 10 or 12 W/kg GSM RFR, and for females exposed to 12 W/kg GSM RFR. As noted in Supplemental Tables S11 and S12, mean body temperatures were significantly decreased in most groups of young and aged, male and female rats, as well as pregnant female rats exposed to higher levels of GSM and CDMA RFR at 2 days, 4 days, or both. Decreases in body temperature were not seen in mice exposed to GSM or CDMA (Supplemental Tables S13 and S14).

DISCUSSION

Studies were conducted in groups of young and aged rats and mice and in pregnant rats to determine the effects of animal size and pregnancy status on the thermal response to RFR. In pregnant dams and aged male and female Harlan Sprague–Dawley rats, exposure to 10 and 12 W/kg GSM or CDMA RFR at 900 MHz for approximately 9 h a day for 5 consecutive days induced increases in body temperature. In many cases of aged male rats, increased body temperature resulted in mortality. In general, aged rats were more sensitive to the heating effects of RFR exposure than smaller, young rats. In young male and female rats, exposure to GSM or CDMA RFR at 10 and 12 W/kg significantly increased mean body temperatures, but no mortality was observed. Despite the age difference between the rats exposed to GSM (38 weeks) and CDMA (22 weeks), the observed changes in body temperature were similar. This likely reflects the similarity in body weights (Table 1). At exposures of 8 W/kg GSM or CDMA RFR, significant increases in body temperature were also observed in pregnant dams and aged rats, with several instances considered to be excessive (>1 °C) increases above controls. Fewer incidences of increases and less severe increases in body temperature were observed at 8 W/kg in young rats than in older rats. At 6 W/kg, there were some incidences of increased body temperature in older male and female rats exposed to GSM or
CDMA RFR, but not in young rats. Sporadic instances of increased body temperature that were not considered to be exposure-related were observed at 4 W/kg GSM or CDMA RFR.

It is widely accepted that exposure to RFR can result in temperature increases in biological tissues and if excessive, result in the disruption of thermoregulation in animals. However, the extent of heating effects depends on the animal (age/size, species, and strain) and parameters of the RF signal (power level, frequency, modulation). As observed in the current studies, larger rats were more sensitive than smaller rats of the same strain. Male rats, which are larger than females, were more sensitive to RFR-induced increases in body temperature compared to females. When compared to the effects in mice, rats were more sensitive to RFR-induced increases in body temperature. These differences could be attributable to several factors, including animal mass, surface area, species-specific differences in thermoregulation, and differences in exposure frequencies between rats (900 MHz) and mice (1,900 MHz). Gong et al. [2017] showed that RFR absorption in rats at 900 MHz was greater than at 1,900 MHz, and conversely absorption in mice was greater at 1,900 MHz than at 900 MHz.

Other studies have reported RFR-induced changes in body temperature and increased mortality for rats and mice exposed to similar types of RFR as in the current studies at levels ranging from 4 to 20 W/kg SAR [Smith et al., 2007; Klose et al., 2014; Ohtani et al., 2016]. The thermal breakdown threshold is the point at which there is an increase in body temperature that exceeds the animal’s capacity to dissipate heat. Thermal breakdown thresholds of 7.7 to 11.5 W/kg have been reported for different strains of rats [Lu et al., 1987]. These are consistent with the results observed in the current studies of RFR with Sprague–Dawley rats.

As opposed to the rats, exposures in the current study did not extend high enough to observe the thermal breakdown threshold in B6C3F1 mice. While studies conducted by Ebert et al. [2005] demonstrated thermal breakdown thresholds of 10.1 W/kg in B6C3F1 mice and 7.7 W/kg in NMRI mice, the differences may be attributable to differences in exposure conditions. It is important to note that in the current study, exposures were conducted in free-moving, unrestrained mice, with a 10 min on, 10 min off exposure pattern, as opposed to mice that were restrained in plastic tubes during 2 h of continuous RFR exposure as in the Ebert et al. [2005] studies.

In pregnant rats, there was a significant effect of GSM RFR on the number of resorptions observed at 12 W/kg GSM RFR. No treatment-related effects on pregnancy were observed in rats exposed to CDMA RFR, although body temperatures were increased.

There was a rebound decrease in body temperature in most groups of rats when measured 3 h after exposure cessation. These decreases tended to occur in groups where increased body temperatures were observed immediately after exposure. The reasons for the generally lower body temperature following a recovery period are not known, but could be due to a thermoregulatory adaption of the animal.

Based on the results from these pilot studies, 28-day prechronic studies were designed to evaluate the short-term toxicity of exposure to GSM- and CDMA-modulated RFR and determine appropriate exposures for the subsequent 2-year chronic studies. As a result of the increased mortality and excessive increases in body temperature observed in the current studies, SARs of ≥10 W/kg GSM or CDMA RFR were not considered for subsequent studies in Harlan Sprague–Dawley rats. The SAR levels selected for the prechronic perinatal toxicology studies in rats were 0, 3, 6, and 9 W/kg. Only sporadic increases in body temperature were observed in young and old male and female mice exposed to GSM or CDMA RFR up to 12 W/kg, suggesting that mice could tolerate SARs >12 W/kg. Therefore, the upper SAR level for the prechronic toxicology studies in mice was limited by the power constraints of the exposure facility to a maximum of 15 W/kg, and lower SAR levels set at 0, 5, and 10 W/kg.

REFERENCES

Anderson LE, Sheen DM, Wilson BW, Grumbein SL, Creim JA, Sasser LB. 2004. Two-year chronic bioassay study of rats exposed to a 1.6 GHz radiofrequency signal. Radiat Res 162:201–210.

Bartsch H, Kupper H, Scheurlen U, Deerberg F, Seebald E, Dietz K, Mecke D, Probst H, Stehle T, Bartsch C. 2010. Effect of chronic exposure to a GSM-like signal (mobile phone) on survival of female Sprague–Dawley rats: Modulatory effects by month of birth and possibly stage of the solar cycle. Neuro Endocrinol Lett 31:457–473.

Capstick MH, Kuster N, Kühn S, Berdinas-Torres V, Gong Y, Wilson P, Ladbury J, Koepke G, McCormick D, Gauger J, Melnick R. 2017. A radio frequency radiation reverberation chamber exposure system for rodents. IEEE Trans EMC 59:1041–1052.

Cellular Telecommunications Industry Association. 2017. “Americans’ Wireless Data Usage Continues to Skyrocket.” https://www.ctia.org/industry-data/ctia-annual-wireless-industry-survey. [Last accessed 18 December 2017].

Chou CK, Guy AW, Kunz LL, Johnson RB, Crowley JJ, Krupp JH. 1992. Long-term, low-level microwave irradiation of rats. Bioelectromagnetics 13:469–496.
Ebert S, Eom SJ, Schuderer J, Apostel U, Tillmann T, Dassenbrock C, Kuster N. 2005. Response, thermal regulatory threshold and thermal breakdown threshold of restrained RF-exposed mice at 905 MHz. Phys Med Biol 50:5203–5215.

Frei MR, Berger RE, Dusch SJ, Guel V, Jauchem JR, Merritt JH, Stedham MA. 1998a. Chronic exposure of cancer-prone mice to low-level 2450MHz radiofrequency radiation. Bioelectromagnetics 19:20–31.

Frei MR, Jauchem JR, Dusch SJ, Merritt JH, Berger RE, Stedham MA. 1998b. Chronic, low level (1.0 W/kg) exposure of mice prone to mammary cancer to 2450 MHz microwaves. Radiat Res 150:568–576.

Gong Y, Capstick MH, Kühn S, Wilson P, Ladbury J, Koepke G, McCormick D, Melnick R, Kuster N. 2017. Life-time dosimetric assessment for mice and rats exposed to cell phone radiation exposed in reverberation chambers. IEEE Trans EMC 59:1798–1808.

Gong Y, Capstick M, Tillmann T, Dassenbrock C, Samaras T, Kuster N. 2016. Desktop exposure system and dosimetry for small scale in vivo radiofrequency exposure experiments. Bioelectromagnetics 37:49–61.

Klose M, Grote K, Spathmann O, Strecker J, Clemens M, Hansen VW, Lerchl A. 2014. Effects of early-onset radiofrequency electromagnetic field exposure (GSM 900 MHz) on behavior and memory in rats. Radiat Res 182:435–447.

La Regina M, Moros EG, Pickard WF, Straube WL, Baty J, Roti JL. 2003. The effect of chronic exposure to 835.62MHz FDMA or 847.74MHz CDMA radiofrequency radiation on the incidence of spontaneous tumors in rats. Radiat Res 160:143–151.

Lee HJ, Jin YB, Lee JS, Choi SY, Kim TH, Pack JK, Choi HD, Kim N, Lee YS. 2011. Lymphoma development of simultaneously combined exposure to two radiofrequency signals in AKR/J mice. Bioelectromagnetics 32:485–492.

Lin JC. 2017. Cancer occurrences in laboratory rats from exposure to RF and microwave radiation. IEEE J-ERM 1:2–13.

Lu S-T, Lebda NA, Lu S-J, Pettit S, Michaelson SM. 1987. Effects of microwaves on three different strains of rats. Radiat Res 110:173–191.

National Research Council. 1996. Guide for the Care and Use of Laboratory Animals. Washington, DC: The National Academies Press.

Oberto G, Rolfo K, Yu P, Carbonatto M, Peano S, Kuster N, Ebert S, Tofani S. 2007. Carcinogenicity study of 217 Hz pulsed 900 MHz electromagnetic fields in Pim1 transgenic mice. Radiat Res 168:316–326.

Ohtani S, Ushiyama A, Maeda M, Hattori K, Kunugita N, Wang J, Ishii K. 2016. Exposure temperature-dependent thermal effects of radiofrequency electromagnetic field exposure on the whole body of rats. J Toxicol Sci 41:655–666.

Pew Research Center. 2013. “Cell Phone Ownership Hits 91% of Adults.” http://www.pewresearch.org/fact-tank/2013/06/06/cell-phone-ownership-hits-91-of-adults/. [Last accessed 8 December 2017].

Repacholi MH, Basten A, Gebski V, Noonan D, Finnie J, Harris AW. 1997. Lymphomas in Eμ-Pim1 transgenic mice exposed to pulsed 900 MHz electromagnetic fields. Radiat Res 147:631–640.

Saran A, Pazzaglia S, Mancuso M, Rebessi S, Di Majo V, Tanori M, Lovisolo GA, Pinto R, Marino C. 2007. Effects of exposure of newborn patched1 heterozygous mice to GSM, 900 MHz. Radiat Res 68:733–740.

Smith P, Kuster N, Ebert S, Chevalier H-J. 2007. GSM and DCS wireless communication signals: Combined chronic toxicity/carcinogenicity study in the Wistar rat. Radiat Res 168:480–492.

Sommers AM, Bitz AK, Strecker J, Hansen VW, Lerchl A. 2007. Lymphoma development in mice chronically exposed to UMTS-modulated radiofrequency electromagnetic fields. Radiat Res 168:72–80.

Sommers AM, Strecker J, Bitz AK, Hansen VW, Lerchl A. 2004. No effects of GSM-modulated 900 MHz electromagnetic fields on survival rate and spontaneous development of lymphoma in female AKR/J mice. BMC Cancer 4:77–90.

Tillmann T, Ernst H, Ebert S, Kuster N, Behnke W, Rittinghausen S, Dassenbrock C. 2007. Carcinogenicity study of GSM and DCS wireless communication signals in B6C3F1 mice. Bioelectromagnetics 28:173–187.

Toler JC, Shelton WW, Frei MR, Merritt JH, Stedham MA. 1997. Long-term, low-level exposure of mice prone to mammary tumors to 435MHz radiofrequency radiation. Radiat Res 148:227–234.

Utteridge TD, Gebski V, Finnie JW, Vernon-Roberts B, Kuchel TR. 2002. Long-term exposure of Eμ-Pim1 transgenic mice to 898.4MHz microwaves does not increase lymphoma incidence. Radiat Res 158:357–364.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article at the publisher’s website.