RESEARCH

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EXPERIMENTAL IDENTIFICATION OF POSSIBLE HEALTH HAZARDS ASSOCIATED WITH EXPOSURE TO RADIOFREQUENCY RADIATION

The NTP Cell Phone RF Toxicology Program at IIT Research Institute

Identification of chemical or physical agents with potential carcinogenic activity in humans is ideally based on a "sum of the evidence" approach in which the results of epidemiology studies performed in exposed human populations are integrated with data from experimental bioassays of carcinogenicity conducted in validated laboratory animal models. Hazard identification data from epidemiological and experimental studies are often supplemented with, and can be considerably strengthened by, mechanistic investigations that are designed to identify possible cellular, biochemical, or molecular mechanisms of carcinogenic action.

Although the body of published epidemiologic studies investigating possible links between exposure to radiofrequency radiation (RF) generated by mobile telephones and human cancer risk continues to expand, no overall consensus has emerged. Most epidemiology studies have failed to identify any statistically significant link between the use of mobile telephones and cancer risk; however, increases in cancer risk have been reported in a number of studies, and questions remain concerning possible adverse effects of exposure to mobile telephone RF in sensitive subpopulations (such as children and young adults) and in individuals who are exposed over long periods of time (> 10 years).

Animal experiments in comparison with other study types

In situations where epidemiology does not support the conclusive identification and quantitation of the potential risks associated with exposure to an agent, laboratory studies conducted in appropriate experimental model systems increase in importance. Well-designed and controlled animal studies permit evaluation of biological effects in vivo under tightly controlled exposure and environmental conditions, and in the absence of potential confounding variables. Particular strengths of laboratory investigations of the possible hazards of RF exposure include (a) precise

definition, control, and monitoring of the RF metrics under investigation; (b) ability to perform mechanistic studies of agent action in parallel with the conduct of the hazard identification bioassays; and (c) control of extrinsic factors that could alter responses to the RF metric. Conversely however, studies in experimental model systems require an interspecies extrapolation of data to evaluate human risk, and may also require extrapolation from the dose levels used in the bioassay to the (often much lower) doses to which humans may be exposed.

In consideration of the conflicting results of epidemiology studies of mobile phone use and cancer, and difficulties associated with exposure assessment in such studies, well-conducted studies in animal model systems can provide data that are critical to identifying possible hazards that may result from exposure to RF.

Mobile phone studies within the NTP

To investigate the possible health effects of RF exposure in a series of well-validated laboratory animal models, a program entitled “Studies to Evaluate the Toxic and Carcinogenic Potential of Cell Phone Radiofrequency Radiation” is currently in progress at IIT Research Institute (IITRI) in Chicago. This program is supported by funding from the National Toxicology Program (NTP) of the National Institute of Environmental Health Sciences, United States National Institutes of Health.

Experimental work is being performed at IITRI in a custom-design and constructed RF exposure facility that is fully dedicated to the NTP RF Toxicology Program. The IITRI RF exposure facility occupies approximately 1600 square meters, and is operated as a full barrier animal laboratory. RF exposures are performed using 21 reverberation chambers (14 for rats, 7 for mice; Figure 1) that were designed, constructed, and installed by IT’IS Foundation, Zurich, Switzerland. Each chamber holds two non-metallic animal cage racks, and has a total capacity of 120 Sprague-Dawley rats or 224 B6C3F1 mice. Environmental conditions and RF signal characteristics are continuously monitored in each RF exposure chamber; performance of the RF exposure and monitoring system has been independently validated by the U.S. National Institute of Standards and Technology (NIST).

In all studies, parallel groups of animals receive either sham exposure; whole body exposure to GSM signals (3 different signal strengths); or whole body exposure to IS-95 signals (3 different signal strengths). In consideration of interspecies scaling factors, rats are exposed to 900 MHz GSM or IS-95 signals, and mice are exposed to 1900 MHz GSM or IS-95 signals. Animals are exposed to RF signals (10 minutes on, 10 minutes off) for

Delivery of an exposure unit at IITRI

Installation of an exposure unit (reverberation chamber)

RF reverberation chambers at IITRI

18.5 hours per day, 5 days per week. Animals are never restrained, and are housed unrestrained in their home cages at all times during the studies. All studies are performed in strict compliance with United States Food and Drug Administration Good Laboratory Practice (FDA-GLP) regulations.

Different study parts

The first study in the program is a pilot study to determine the relationship between RF field strength and thermal responses. It is well known that cataracts and other adverse health effects are induced by tissue heating. However, because generalized increases in body temperature have not been reported in humans as a result of the use of mobile telephones, it is essential that the toxicity and oncogenicity studies in animal models be performed using RF power levels that do not increase body temperature.

View into an exposure chamber with animal cage racks

The goal of the Thermal Pilot Study is to identify the maximum Specific Absorption Rate (SAR) to which young mice, young rats, aged mice, aged rats, and pregnant rats can be exposed without increasing body temperature by more than 1 oC. This study has been completed, and its results used to set RF exposure levels for subsequent studies.

The *Thermal* Pilot Study is followed by *Perinatal/Prechronic* Toxicity Studies, in which a battery of toxicologic evaluations (survival, body weight, clinical observations, clinical pathology, gross and microscopic pathology) is performed in rats and mice to identify any adverse effects of short term, repeat dose exposure to RF. These studies also include specialized evaluations to identify possible effects of RF exposure on the integrity of the blood-brain barrier, and to characterize the effects of RF exposure on patterns of gene expression.

In the *perinatal/prechronic* studies, rats are exposed beginning in utero (at gestation day 6), and are exposed continuously throughout gestation, parturition, and for 7 weeks after delivery. Young adult mice are exposed of RF for four weeks. These studies are currently in progress, and will provide data concerning possible effects of short-term, repeat-dose exposure to RF fields. The results of the perinatal/prechronic toxicity studies will also be used to support the selection of RF exposure levels for the chronic studies.

The final studies to be conducted in this program are chronic toxicity/oncogenicity evaluations; these studies will be 2011, with final report submission expected in 2014. In these studies, groups of rats and mice (100 per sex per species per group) will be exposed to RF for up to 2 years, beginning at the same time points used in the prechronic studies. Although the chronic studies include in-life toxicology observations, their most critical component is the histopathologic evaluation of tissues. A comprehensive microscopic evaluation will be performed on approximately 50 tissues from each study animal; in consideration of the group sizes in the chronic studies and the breadth of the histopathology to be performed, these studies will provide the most comprehensive evaluation of the chronic toxicity and possible oncogenicity of RF fields that has been performed to date.

The final report ot this NTP research program is expected in 2014.

Special characteristics of this investigation

The design of these chronic toxicity/oncogenicity studies differs from previously reported chronic studies of RF in several important ways:

- RF exposures in rat studies are initiated during the gestation period, and continue throughout the juvenile and adult periods. As such, these studies are designed to identify possible differential sensitivity to RF that may be seen in the fetus, neonatal animals, or juvenile animals.
- Animals are not restrained at any time during RF exposures, thus reducing animal stress and any possible confounding effects of stress hormones.
- The lack of animal restraint means that animals can be exposed for longer periods (18.5 hours) per day, rather than the shorter periods necessary in studies in which animals are restrained.
- Because animals are not restrained in these studies, RF exposures are whole-body, rather than head-only.
- The very large group size and extensive plan for histopathologic evaluation of tissues confers a statistical power to these studies that exceed that of prior investigations.

FURTHER INFORMATION

NTP Project Website

- *http://ntp.niehs.nih.gov/ntpweb/index.cfm?objectid=7E733ABE-BDB5-82F8-FBDC3F58C-0CEE928*

IT'IS Website

- *http://www.itis.ethz.ch/research/em-exposure-health/health-risk-assessment/*

Author

David McCormick is Senior Vice-President and Director of IIT Research Institute, and Professor of Biology at the Illinois Institute of Technology in Chicago. A board-certified toxicologist, McCormick has particular expertise in studies of carcinogenesis, drug development for cancer prevention and therapy, and the biological effects of magnetic fields. He currently serves as Principal Investigator for the NIEHS/NTP program entitled "Studies to Evaluate the Toxic and Carcinogenic Potential of Cell Phone Radiofrequency Radiation", and previously served the same role in the NIEHS/NTP Program entitled "Studies to Evaluate the Toxic and Carcinogenic Potential of 60 Hz Magnetic Fields in Laboratory Animals". He received his Ph.D. in Environmental Medicine/Biology from the Institute of Environmental Medicine at New York University.

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