

Use of Experimental Models to Identify Possible Health Effects of Exposure to RF Fields

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Question

Does exposure to radiofrequency radiation from cell phones or other wireless communications devices increase the risk of cancer or other adverse health outcome?

Epidemiology (Case-Control)

Inskip, Linet *et al.*, New Engl. J. Med (2001)

- No association with brain tumor risk; study not designed to evaluate risks of long-term heavy use.

Linet *et al.*, Inter. J. Cancer (2006)

- No overall association with risk of lymphoma.

Kan *et al.*, J. Neurooncology (2008)

- No overall association with brain cancer risk; significantly increased risk (OR: 1.25) for ≥ 10 years of use (meta-analysis of case-control studies).

Epidemiology - Conclusions

General Consensus

- No compelling body of epidemiologic evidence supports an increased risk of any type of neoplasm or other health effect.

However, important questions remain:

- Is risk of adverse health effects increased with **long-term** use of cell phones?
- Is risk increased in **sensitive sub-populations**?

Challenges to RF Hazard Identification

Limitations to Epidemiology (General)

- exposure assessment (recall bias)
- limited sensitivity to detect quantitatively small effects superimposed on a finite background
- temporal variability of exposures: when is the “critical period” for exposure?

Challenges to RF Hazard Identification

Limitations to Epidemiology (RF-specific)

- exposure assessment: what is the relevant RF exposure metric?
- limited duration of exposure in study populations
- unknown relative sensitivity of children or other potentially susceptible subpopulations

Challenges to RF Hazard Identification

Issues Associated with Sole Reliance on Epidemiology Data to Identify Health Hazards:

- Latency of hazard development
- Time required to identify hazards through epidemiology (*post-hoc* evaluation)

Application of Experimental Data to Human Hazard Identification

Where epidemiology data are inadequate or are inconclusive, well-designed studies in experimental models may provide data that are critical to the rational identification of human health hazards.

Application of Experimental Data to Human Hazard Identification

Assessment of the possible hazards associated with human exposure to cell phone radio-frequency fields provides an ideal example of such a situation.

Application of Experimental Data to Human Hazard Identification

Challenges to Experimental Approaches

- high dose to low dose extrapolation
- interspecies extrapolation
- relevance of exposure metric
- study power (usually limited by study logistics)

Application of Experimental Data to Human Hazard Identification

What do experimental
studies tell us?

Overview of US RF Data

Adey *et al.*, Rad Res (1999); Cancer Res (2000)

TDMA (836 MHz): 2 year oncogenicity, ENU.

Zook and Simmens, Rad Res (2001, 2006)

TDMA (860 MHz): 2 year oncogenicity, ENU.

Roti-Roti *et al.*, Rad Res (2003) – FDMA [835

MHz] or CDMA [847 MHz]: 2 year oncogenicity

Anderson *et al.*, Rad. Res. (2004) – IRIDIUM

signal [1616 MHz]: 2 year oncogenicity

Issues in Experimental Studies

Group Size and Statistical Power

Relevance of Exposure Metrics (evolution of cell phone RF signals over time)

Experimental Considerations

- generation and monitoring of RF signals
- exposure duration (hrs per day, days per week)
- animal restraint during exposure
- are specific subpopulations differentially sensitive to RF effects?

**Studies to Evaluate the Toxic
and Carcinogenic Potential of
Cell Phone Radio Frequency
Radiation in Laboratory
Animals for the National
Toxicology Program (NTP)**

Principal Collaborators

- IIT Research Institute (Chicago)
 - Thomas L. Horn, Ph.D., D.A.B.T. – Study Director
 - James R. Gauger – Project Engineer
- IT'IS Foundation (Zurich)
 - Niels Kuster, Ph.D. -- Lead Engineer
 - Myles Capstick, Ph.D. – Project Engineer
- NIEHS – NTP (Research Triangle Park)
 - Ronald Melnick, Ph.D. – Project Officer

IITRI Cell Phone RF Laboratory

- ~17,000 square feet (~ 1600 square meters)
- Fully dedicated to Cell Phone RF Project
- Access/return (“clean/dirty”) corridor design
- Laboratory contains:
 - Exposure Chamber Area
 - Quarantine/Breeding Rooms
 - Engineering Control Room
 - Necropsy Laboratory
 - Cage Wash Area
 - Data Office
 - Feed/Bedding and other Storage Areas
 - Locker Rooms

IITRI Cell Phone RF Laboratory

- RF exposure area contains 21 reverberation chambers (14 rat chambers [by sex], 7 mouse chambers)
- Each chamber holds 2 custom-designed racks (chamber capacity: 120 rats or 224 mice)
- Each chamber is continuously monitored for: RF signal characteristics (frequency, intensity), lighting, temperature, humidity, air flows

Exposure Chamber Delivery



Exposure Chamber Delivery



Exposure Chamber Delivery



Exposure Chamber Delivery



Cell Phone Lab Exposure Area



RF Exposure Parameters

- RF Signal Generation:
 - Sprague-Dawley Rats: 900 MHz GSM and CDMA
 - B6C3F1 Mice: 1900 MHz GSM and CDMA
- Exposure systems validated by U.S. National Institute of Standards and Technology (NIST)
- Exposures: 10 minutes on, 10 minutes off, 20 hours per day, 5 days per week
- Studies will be fully compliant with Good Laboratory Practice (GLP) regulations

Thermal Pilot Study

- Goal: Identify maximum RF flux density that will not increase body temperature by > 1 °C
- Exposure Groups: Time-averaged SARS of 4, 6, 8, 10, and 12 W/kg.
 - 5/sex/group/species, 5 weeks of age
 - 5/sex/group/species, 20 weeks of age
 - 5 pregnant dams/group/species, gestation day 10
- Exposure Duration: 5 days

Perinatal/Prechronic Toxicity Study

- Goal: Identify toxic effects of subchronic exposure to non-thermal RF fields
- Exposure Groups: GSM and CDMA exposures at 3 power levels each (selected using data from the Thermal Pilot Study) + controls.
 - 10 pregnant dams/group/species, gestation day 6
 - Litters culled to 4/sex (PND 4), 2/sex (PND 21)
 - Post-lactational exposure (10/sex/species/group) from post-natal day 21 through post-natal day 49

Perinatal/Prechronic Toxicity Study

- In-Life Experimental Endpoints:
 - Survival
 - Clinical Observations
 - Body Weight
 - Body Temperature
- Post-mortem Experimental Endpoints:
 - Organ Weights
 - Microscopic Pathology (all tissues, all animals)
 - Integrity of the Blood-Brain Barrier Integrity (vascular permeability using fluorescent dextrans)
 - Neonatal Brain Morphology
 - Gross Pathology

Chronic Toxicity/Oncogenicity Study

- Goal: Identify toxic and oncogenic effects of chronic exposure to non-thermal RF fields
- Exposure Groups: GSM and CDMA exposures at 3 power levels each (selected using data from the Prechronic Toxicity Study) + controls.
 - 50 pregnant dams/group/species, gestation day 6
 - Litters culled to 4/sex on post-natal day 4,
 - Litters culled to 2/sex on post-natal day 21
 - Post-lactational exposure (105/sex/species/group) from post-natal day 21 until 110 weeks of age

Chronic Toxicity/Oncogenicity Study

- In-Life Experimental Endpoints:
 - Survival
 - Clinical Observations
 - Hematology
 - Body Weight
 - Body Temperature
- Post-mortem Experimental Endpoints:
 - Organ Weights
 - Microscopic Pathology (all tissues, all animals)
 - Gross Pathology

Projected Program Schedule

- Thermal Pilot Study
 - Exposures begin December, 2008
 - Completion in May, 2009
- Perinatal/Prechronic Toxicity Study
 - Exposures begin May, 2009
 - Completion in October, 2009
- Chronic Toxicity/Oncogenicity Study
 - Exposures begin November, 2009
 - Completion in Fall, 2012