

A REVIEW OF COMPLETED AND ONGOING RF BIOEFFECTS RESEARCH RELEVANT TO CANCER RISK ASSESSMENT

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Introduction

Over 180 studies have been initiated using human, animal, and cell culture experimental models to investigate whether exposure to radiofrequency (RF) emissions, specifically from mobile telephony, can cause or promote cancer (Table 1). One hundred fifteen of these studies are now complete, with the vast majority reporting no association with cancer endpoints. A list of these studies including details of exposure, test model, and author's conclusions can be obtained from the WHO website at <http://www.who.int/peh-emf/research/database/en/>. The results of cancer related studies from this database will be used by the International Agency for Research on Cancer (IARC) in 2004/05 to evaluate RF emissions as a potential human carcinogen. In addition, the results of non-cancer related studies from this database will be used by the WHO in 2005/06 to evaluate RF emissions for adverse human health effects other than cancer. In such evaluations, epidemiological studies will carry the most weight. Animal studies will play an important role when epidemiological studies are weak or not definitive. In vitro studies will generally have a supporting or clarifying role.

Observations

Twelve relevant epidemiological studies have been completed and report on the potential for mobile telephone RF exposure to cause brain and other forms of cancer (Table 2). In addition, two studies have been completed that looked at associations between cell phone use and eye melanoma. The majority of these studies report no association with cancer, and although two studies do report marginal effects, these are inconsistent in their findings when compared with each other and with the rest of the studies in the database. A large number of epidemiological studies, many funded by the EU 5th Framework program and organized through IARC, are

currently ongoing to provide further data. In addition, 15 long-term animal bioassays, 20 cancer-initiated animal assays, and 2 tumor cell line injection bioassays have been initiated to look at mobile phone-type RF exposure and cancer (Table 3). Of these animal studies, only one by Repacholi et al (1997) has reported positive results, and this study had a number of shortcomings in the experimental design. The Repacholi study has been unable to be replicated/verified (Utteridge et al 2002) and is currently being replicated in another independent laboratory. Finally, there are a large number of short-term animal and in vitro studies addressing various endpoints related to cancer. The majority of these again report no association between mobile phone-type RF exposure and cancer endpoints, and those that do report positive findings either have not, or cannot, be independently replicated.

Conclusions

The majority of studies investigating potential carcinogenicity of mobile telephony RF emissions show no effects. This has lead numerous expert panels (see Table 4) to conclude that no evidence exists to support RF exposure as an agent that can either initiate or promote cancer. Sporadic studies that have reported an association between mobile telephone RF emissions and various cancer-relevant endpoints do not support one another in any obvious common mechanism, and have all either failed to be replicated in independent laboratories or replication attempts have not been completed to date. No plausible biological mechanism exists to explain how RF energy might interact non-thermally with biological tissue to initiate or promote cancer. If current ongoing studies continue to report no association between RF exposure and cancer endpoints, the available data contained within the WHO database should be more than sufficient for the IARC to make a conclusive carcinogenic evaluation of RF exposure from mobile telephony devices.

Table 1. List of current and completed studies looking at the potential biological effects of exposure to mobile phone-type RF signals.

Type of Study	Completed	Ongoing	Total
➤ Cancer relevant or related			
▪ <i>Epidemiological studies</i>	12	24	36
▪ <i>Standard bioassays</i>	8	7	15
▪ <i>Sensitized in-vivo studies</i>	13	7	20
▪ <i>Acute in-vivo studies</i>	23	8	31
▪ <i>In-vitro studies</i>	57	25	82
➤ Total Cancer Studies	115	69	184
➤ Non-cancer studies			
▪ <i>Epidemiology</i>	10	1	11
▪ <i>Acute in-vivo studies</i>	37	10	47
▪ <i>In-vitro studies</i>	15	7	22
▪ <i>Human studies</i>	50	21	71
➤ Total Non-Cancer Studies	112	39	151
❖ Grand Totals	225	110	335

Table 2. Completed and ongoing epidemiological studies. The WHO ID denotes the access number to the study description in the WHO database at <http://www.who.int/peh-emf/research/database/en/>

Case Control Studies:

PI	End Point	Status	WHO ID
Inskip & Linet	Brain tumor, acoustic neuroma & meningioma incidence in humans (n=700) and cellular telephone use (USA).	No Effect Observed N Engl J Med (2001) 344:79-86	168
Muscat et al	800 & 1900 MHz (cell phone use) and glioblastoma, astrocytoma, acoustic neuroma & salivary gland tumor incidence.	No Effect Observed Neurology (2002) 58:1304-1306 JAMA (2000) 284:3001-3007	220
Hardell et al	Brain tumor incidence and cellular telephone use	Effect Observed Intl J Oncology (2003) 22:399-407; European J Cancer Prevention (2002) 11:377-386; European J Cancer Prevention (2001) 10:1-7; Med Gen Med (2000) 2(2); Intl J Oncology (1999) 15:113-116	229
Auvinen et al	900 & 1800 MHz (GSM & NMT) phone use and analysis of brain and salivary gland tumors.	Marginal Effect Reported Epidemiology (2002) 13:356-359	816

Baumgardt-Elms	900 & 1800 MHz (GSM) exposure from mobile phones & other sources and testicular cancer (data extracted from a larger case control study).	No Effect Observed Cancer Causes and Control (2002) 13:895-902	1040
Warren et al	Mobile phone use (all types) and facial tumor incidence.	No Effect Observed The Laryngoscope (2003) 113(4):663-667	1071
Dunn et al	Cell phone use, base station exposure and analysis of childhood cancer and leukemia incidence (UK program).	Ongoing	764
IARC Coordinated	900 & 1800 MHz (analog & GSM) cell phone use and incidence of brain, head and neck tumors.	Ongoing – 170, 171, 172, 289, 309, 311, 12, 313, 314, 315, 316, 317, 318, & 357	169

Cohort Studies:

PI	Endpoint	Status	WHO ID
Morgan et al	Total cancer incidence in Motorola employees occupationally exposed to RF.	No Effect Observed Epidemiology (2000) 11:118-127	173
Rothman et al	800 & 1900 MHz (cell phone use) and total mortality in the USA.	No Effect Observed Epidemiology (1996) 7(3):303-305	174
Johansen et al	900 & 1800 MHz (GSM) cell phone use and cancer incidence and mortality in Denmark	No Effect Observed JNCI (2001) 93:203-206	176
Cook et al	Ecological correlation study of mobile phone use and brain, head, and neck tumors in New Zealand	No Effect Observed The New Zealand Medical Journal (2003) 116: 1-8	1056
Charlton et al	Ecological correlation study between smoking and mobile phone use in teenagers	Hypothesis Presented (correlation between smoking & mobile phone use) British Med J. (2003) 326:161	1020
De Roos et al	Occupational and mobile phone exposure & neuroblastoma in offspring	No Effect Observed Epidemiology (2001) 12:508-17; Cancer Causes & Controls (1999) 10:539-49	1025
Rothman et al	800 & 1900 MHz (cell phone use) and brain tumor incidence.	On hold	175
Ahn, Yoon-Ok	Cell phone use in Korea and cancer incidence.	Ongoing	837
Elliot et al	Pilot study prior to larger 900 MHz (GSM) cohort in England.	Ongoing	891

Eye Melanoma Studies

PI	Endpoint	Status	WHO ID
Stang et al	900 & 1800 MHz (GSM) cell phone & two-way radio exposures. Case control study of uveal melanoma (eye cancer).	Marginal Effect Reported Epidemiology (2001) 12:7-12	643
Johansen et al	900 & 1800 MHz (GSM) cell phone & two-way radio exposures and incidence of melanoma in the eye.	No Effect Observed British J Cancer (2002) 86:348-349	900
Mitchell & Rose	900 MHz (AMPS, CDMA, GSM) effects on visual and auditory pathology in humans.	Ongoing	721

Table 3. Current completed and ongoing long term animal studies. The WHO ID denotes the access number to the study description in the WHO database at <http://www-nt.who.int/peh-emf/database.htm>.

TwoYear Bioassays:

PI	Endpoint	Status	WHO ID
Adey et al	836.55 MHz (TDMA) exposure in standard rat 2-year bioassay.	No increased tumor formation Rad. Res. (199) 152:293-302	1
Adey et al	836.55 MHz (FM) exposure in standard rat 2-year bioassay.	No increased tumor formation Cancer Res. (2000) 60:1857-63	788
Zook et al	860 MHz (MiRS/TDMA) exposure in standard rat 2-year bioassay.	No increased tumor formation Rad. Res. (2001) 155:572-583	6
Zook et al	860 MHz (FM) exposure in standard rat 2-year bioassay.	No increased tumor formation Rad. Res. (2001) 155:572-583	789
Spalding	800 MHz (CW) exposure on RFM mice.	No increased tumor formation Health Phys. (1971) 20:421-424	423
Roti, Roti et al	835.62 MHz (FM) exposure in standard rat 2-year bioassay.	No increased tumor formation BEMS 2002	9
Roti, Roti et al	847.74 MHz (CDMA) exposure in standard rat 2-year bioassay.	No increased tumor formation BEMS 2002	790
Anderson et al	1616 MHz (IRIDIUM) exposure in standard rat 2-year bioassay.	No increased tumor formation BEMS 2002	11
Dasenbrook et al	900 MHz (GSM) RF exposure for 2 years to B6C3F1 mice.	Ongoing	244
Dasenbrook et al	1800 MHz (DCS) RF exposure for 2 years to B6C3F1 mice.	Ongoing	944
Dotti et al	1800 MHz (DCS) RF exposure for 2 years to Wistar rays.	Ongoing	245

Dotti et al	900 MHz (GSM) RF exposure for 2 years to Wistar rats.	Ongoing	945
Sharai et al	1.5 GHz (PDC) exposure and standard NTP type bioassay	Ongoing	328
Yamaguchi et al	1.5 GHz (PDC) exposure and brain tumors	Ongoing	329

Chemically, Genetically, and Radiation Initiated Bioassays:

PI	Endpoint	Status	WHO ID
Adey et al	836.55 MHz (TDMA & FM) exposure in ENU induced rat brain tumor bioassay.	No increased tumor formation Rad. Res. (1999) 152:293-302; Cancer Res. (2000) 60:1857-63	4
Zook et al	860 MHz (MiRS TDMA & FM) exposure in ENU-induced rat brain tumor bioassay.	No Effect Observed Rad. Res. (2001) 155:572-583	8
Zook et al	860 MHz (MiRS/TDMA & FM) exposure in ENU-induced tumor latency bioassay.	No Effect Observed Radiation Research (in preparation)	7
Chagnaud et al	900 MHz (GSM) exposure in Benz(a)Pyrene induced rat sarcoma	No Effect Observed Int J Radiat Biol (1999) 75(10):1251-6	12
Imaida et al	929 & 1500 MHz (PDC) exposure in DEN induced-GSTp(+) rat hepatoma bioassay.	No Effect Observed Carcinogenesis (1998) 19(2):311-314; Jpn J Cancer Research (1999) 89:995-1002	13
Heikkinen et al	902 MHz (GSM) exposure in radiation induced mouse lymphoma bioassay	No Effect Observed Radiation Research (2001) 156:775-85	15
Heikkinen et al	900 MHz (GSM) exposure on UV induced skin tumors in ODC transgenic & non-transgenic mice	No Effect Observed Int J Radiat. Biol. (2003) 79(4):221-33	16
Bartsch et al	900 MHz (GSM) exposure in DMBA induced rat mammary tumor bioassay	No Effect Observed Radiation Research (2002) 157:183-190	17
Anane et al	900 MHz (GSM) exposure in DMBA induced rat mamary tumor bioassay	No Effects Observed BEMS 2001, St. Paul MN	18
Repacholi et al	900 MHz (PW) exposure on lymphomas in PIM-1 transgenic mice.	Increased mortality Rad. Res. (1997) 147(5):631-640	19
Utteridge et al	900 MHz (PW) exposure on lymphomas in PIM-1 transgenic mice.	No Effects Observed Radiation Research (2002) 158:357-364; Radiation Research (2003) 159:274-278	20
Sykes, P. et al	900 MHz (GSM simulated) exposure on intra-chrom. recomb. in pKZ-1 transgenic mice.	Inconclusive Preliminary Findings Rad. Res. (2001) 156:495-502	21
Persson et al	900 MHz (GSM) exposure to GFAP (-/-) knockout mice on tumor development, micronuclei formation, ODC activity &	No effect BEMS (1999)	287

	polyamine/histamine levels.		
Imaida, . et al	1.5 GHz (PDC) exposure of mice and promotion of skin tumorogenesis in DMBA initiated model.	No effect BEMS (2001)	768
Hruby et al	Replication of DMBA initiated mammary tumor bioassay	Ongoing	246
Oberto, G. et al	Replication of PIM-1 transgenic mouse study for lymphoma development	Ongoing	247
Juutilainen et al	900 MHz (GSM) exposure of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone initiated mice and analysis of tumor formation	Ongoing	323
Chiang Huai	900 MHz (GSM) exposure on DMBA initiated rats and analysis of mammary tumors	Ongoing	593
Lee J-S et al	848. 5 MHz and 1762. 5 MHz RF exposure to hsp70.1 knockout and p53 knockout mice and analysis of histopathology, gene expression, and stress response	Ongoing	994
Shirai et al	2.2 GHz exposure on the promotion of ENU induced brain tumors in rats	Ongoing	1050

Tumor Cell Line Injection Studies:

PI	Endpoint	Status	WHO ID
Salford, L. et al	915 MHz (FM) exposure on RG2 injected brain tumor progression in rats.	No Effect Observed Bioelectrochem. & Bioenergetics (1993) 30:313-318	22
Higashikubo et al	847.74 MHz (CDMA) & 835.62 MHz (FM) exposure on 9L injected brain tumor progression in rats.	No Effect Observed Rad. Res. (1999) 152:665-671	23

Table 4. Some of the Expert Panels/Government Agencies that conclude no evidence exists to support RF exposure can either initiate or promote cancer.

National Radiological Protection Board (NRPB): 1993, 1999, 2003
The International Commission on Non-Ionizing Radiation Protection (ICNIRP): 1996, 1998

<http://www.nrpb.org.uk/>
<http://www.icnirp.de/>

European Commission Expert Group: 1996

<http://europa.eu.int/>

Royal Society of Canada: 1999, 2001

<http://www.rsc.ca/>

UK Independent Expert Group on Mobile Phones (IEGMP - Stewart Report): 2000

<http://www.iegmp.org.uk/>

Health Council of the Netherlands: 2000, 2002

<http://www.gr.nl/>

World Health Organization 2000

<http://www.who.int/peh-emf/en/>

American Cancer Society 2001

<http://www.cancer.org/docroot/home/index.asp>

French Expert Group ('Zmirou'): 2001, 2003

<http://www.sante.gouv.fr/>

Singapore Health Sciences Authority 2001
German Commission for Radiation Protection (SSK): 2001
European Committee on Toxicology, Eco-toxicology and the Environment (CSTEE): 2001, 2002
Swedish Radiation Protection Authority: 2002
Australian Radiation Protection & Nuclear Safety Agency 2002
Norwegian Radiation Protection Authority: 2003
Hong Kong – Office of Telecommunications Authority 2003
US Food and Drug Administration 2003

<http://www.hsa.gov.sg/>
<http://www.ssk.de/>
<http://europa.eu.int/>
<http://www.ssi.se>
<http://www.arpana.gov.au/>
<http://www.nrpa.no>
<http://www.ofta.gov.hk>
<http://www.fda.gov/cellphones/>

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All references, as well as a complete description of the study model and the investigators general conclusions, can be obtained at the WHO database website at <http://www.who.int/peh-emf/research/database/en/> by using the WHO ID number.

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