Background on Radiofrequency Electromagnetic Radiation and Health

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October 11, 2019

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Introduction

This note is intended to provide general background information on radiofrequency electromagnetic radiation (EMR) and health. The sources for it include the 2011 Volume 102 of the International Agency for Research on Cancer (IARC), *Non-Ionizing radiation, Part 2: Radiofrequency Electromagnetic Fields* (I chaired the Working Group for IARC that produced this volume), as well as subsequent literature reviews (https://publications.iarc.fr/126). This note is not based on a comprehensive review of the literature, but citations are included to some key sources.

Readers should recognize that the health risks of EMR are controversial with a range of opinion that spans from the view that there are no confirmed adverse effects of EMR to the contrasting view that EMR causes cancer and possibly other adverse health effects. The literature on EMR and health is substantial with a total of 20,014 citations identified through a search of the medical literature in October, 2019 when this note was written.

An Overview of Radiation

Radiation comprises energy moving in the form of electromagnetic waves or as particles emitted from radioactive isotopes, e.g., alpha particles. EMR is part of the spectrum of electromagnetic radiation, occupying a band of particular frequencies (recall that electromagnetic radiation is describe by the frequency of the waves and their wavelengths) (Figure 1). The energy delivered by radiation depends on the frequency and lower-frequency radiation does not deliver enough energy to tissues to cause ionization and hence is referred to as non-ionizing radiation.

Ionizing radiation is known to cause cancer. The energy that it delivers to tissue is sufficient to injure cells and to damage DNA, causing mutations that underlie the development of cancer. Studies of populations exposed to ionizing radiation, most notoriously the survivors of the atomic bombs dropped on Hiroshima and Nagasaki, provide convincing evidence that ionizing radiation causes most types of cancer and that the risk increases with the dose received. Beyond the studies of the atomic-bomb survivors, the studies include radiation-exposed workers and persons receiving radiation for various medical purposes.

The EMR from cell phones and other sources, however, does not cause such cellular injury and damage to DNA because of the energy delivered. Accordingly, some argue that cancer could not be produced by exposure to EMR from cell phones and other telecommunications devices. Thus, there is uncertainty as to how EMR might cause cancer or other diseases.

How do we study the health effects of EMR?

As for other environmental agents, the work on potential risks posed by EMR have been investigated by exposing cells to EMR to understand possible mechanisms by which EMR could cause disease; by exposing animals to EMR to search for responses and to assess if EMR causes cancer in animals; and finally by carrying out epidemiological (human population) studies of people exposed to EMR, seeking to determine whether there is increased risk for cancer or other diseases from EMR exposure. General descriptions of these approaches follow:

- Cellular/in vitro: Various experimental approaches have been used to understand how EMR may interact with and injure cells, particularly the DNA in cells. Changes to DNA are a hallmark of cancer. Ionizing radiation, a long-established cause of cancer, cause changes in DNA that lead to mutations in the DNA. Some work seeks to determine if EMR has a similar effect.

- Animal bioassay: This type of assessment involves exposure of living animals to EMR with evaluation of tissues for evidence of injury, the occurrence of cancer or other adverse effects. In this type of assessment, one or more species of animals are exposed to EMR generally with a control or sham-exposed group. With this type of assessment, exposure can be tightly controlled, along with other factors that could complicate the findings on EMR, and tissues can be fully examined. With current animal models, it is possible to create animals that mimic human susceptibility. However, generalizing results to people can be uncertain and findings may results may differ from species to species or by sex.

- Epidemiology: Epidemiology comprises the scientific methods used to study the occurrence of diseases and their causes. To date, epidemiological studies have been a mainstay of the research on cancer risks from EMR and particularly from cell phone usage. Two designs have been employed: the case-control design involving identification of people with the disease outcome of concern, the cases, (e.g., people with brain cancer) and similar people with the disease, the controls. The exposures of the two groups are then compared; studies with this design provided the first evidence that smoking causes lung cancer. The second design is the cohort study, which involves follow-up of people over time with tracking of the occurrence of the disease(s) of interest in relation to the exposures received. For example, several studies are in progress that follow people over time with monitoring for the occurrence of brain cancer and tracking of cell phone use through records of cell phone usage. With this design, a comparison can be made between those using cell phones more frequently with those using their phones less frequently.

Evidence integration to determine what is known and not known

A critical step in evaluating the risk of an environmental agent, such as EMR, is to integrate the available evidence to determine what is known; one key question is often whether the agent causes a disease or other adverse effect while another may be how risk varies with the magnitude or level of exposure—that is, is there a dose-response relationship and what is the form of that relationship. For addressing these questions, the most informative approach is to bring together all lines of evidence to judge the what is known. This kind of determination is generally done by expert panels, following guidelines for evidence integration. Such guidelines have long been in use, dating back to the 1960s when burgeoning research findings indicated that smoking caused lung cancer. The 1964 report of the Surgeon General on Smoking on Health, for example, reached the momentous conclusion that cigarette smoking caused lung cancer (in men) (https://biotech.law.lsu.edu/cases/tobacco/nnbbmq.pdf) That conclusion was based on a formal review of evidence and synthesis of different kinds of evidence according to guidelines that remain in use.

For determining whether an environmental agent causes cancer, this type of integrative, transparent approach has long been the standard. Individual scientists and others may offer their views on the state-of-the-science, but generally it is the conclusions of broad-based and systematic reviews of research and other evidence that guide evidence-based decision-making.

The International Agency for Research on Cancer (IARC)

This agency, located in Lyon, France, is the WHO agency charged with addressing cancer (https://www.iarc.fr). Among its components is the IARC Monographs on the Identification of Carcinogenic Hazards to Humans (https://monographs.iarc.fr/). This program, now in existence for five decades, systematically reviews and evaluates all evidence related to environmental agents considered of sufficient significance to undergo such a rigorous assessment. The reviews proceed according to a specified protocol set out in a preamble to each volume; the Preamble was revised in 2019 (https://monographs.iarc.fr/iarc-monographs-preamble-preamble-to-the-iarc-monographs/). To date, IARC has reviewed more than 1000 agents, including radiofrequency electromagnetic fields.

The IARC conclusion with regard to EMR

The agency's Volume 102, *Non-Ionizing Radiation, Part 2: Radiofrequency Electromagnetic Fields*, reached the conclusion that EMR was a Group 2B carcinogen, i.e., a *possible* carcinogen.[1] That conclusion, as described by IARC, was reached on the basis of evidence considered to be *limited* in experimental animals and also in humans. The epidemiological evidence supporting the *limited* designation came from two studies of the case-control design. Such studies are subject to limitations, but the Working Group that developed the report found that potential problems with the studies were not sufficient to account for the finding of an association of cell phone use with increased risk for brain cancer. Some animal bioassays also provided positive findings.

What does the Group 2B classification mean?

Per the IARC Preamble at the time of Monograph 102, "This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals." The Preamble goes on to describe some other combinations of evidence that might be sufficient for this classification. Higher levels of strength of evidence would lead to classification in "*Group 1: The agent is carcinogenic to humans*" or "*Group 2A: The agent is probably carcinogenic to humans*". To date, 120 agents have been placed in Group 1, 82 in Group 2A, and 311 in Group 2B. Five hundred have been classified Group 3, "not classified."

In a landmark 1976 book, Lowrance defined safety as follows: "A thing is safe if its risks are judged to be acceptable."[2] This definition implies that we need to have an understand of what risks are posed, a matter for scientific research, and a judgment as to acceptability, a societal matter. In this context, Group 2B implies that there is substantial uncertainty but an indication that the agent may be a cause of cancer; that is, the evidence indicates the possibility of some risk. In my words, the evidence provides a warning that some risk may exist. Judgment as to the acceptability of risk is clouded by the uncertainty in the characterization of risk. In the face of such uncertainty principles of risk management became paramount, particularly with regard to the precautionary principle—being as protective as possible in the setting of uncertainty.

New evidence since the 2011 IARC Monograph

Since 2011, research on EMR has continued. In a 2014 follow-up to the 2011 report, authors from IARC and myself addressed some new studies and also the challenges of communicating the implications of a Group 2B classification.[3]

Of the new evidence, the most significant may be the completion of two large bioassays: one by the National Toxicology Program (NTP) of the National Institute for Environmental Health Sciences (separate ref #s (https://ntp.niehs.nih.gov/whatwestudy/topics/cellphones/index.html?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=cellphone)[4,5] and the second by the Ramazzini Institute in Italy (https://www.sciencedirect.com/science/article/pii/S0013935118300367?via%3Dihub#t0005).[6] The NTP bioassay involved rats and mice exposed to EMR in a protocol mimicking exposure to 2G and 3G generation EMR. The Ramazzini Institute bioassay used rats that were exposed to EMR reflecting exposure at the base of a cell tower emitting GSM frequency EMR. The results are summarized in Figure 2 and in Tables 1 and 2, taken from reports on the findings. Importantly, the results of both bioassays indicate effects, including the production of tumors involving cells of the nervous system. For example, in both bioassays, unusual tumors of the heart were observed: schwannomas originating from Schwann cells, a type of cell of the nervous system.

The findings are notable for the observation that responses were observed involving cells of the nervous system, including tumors. While the underlying mechanism(s) is uncertain, the observations support the plausibility of adverse effects in humans involving the nervous system, the complexities of interpreting the bioassay results and extending them to people are clear. There are species differences and difference in responses by sex in the rats. Schwannomas are extraordinarily rare in people.

Other studies have been published covering a broad range of health outcomes. The results of one major study of childhood cancer are still pending, the Mobi-Kids Study (https://www.isglobal.org/en/-/mobi-kids-risk-of-brain-cancer-from-exposure-to-radiofrequency-fields-in-childhood-and-adolescence).

IARC has announced its intention to re-review EMR in approximately five years.

Figure 1.
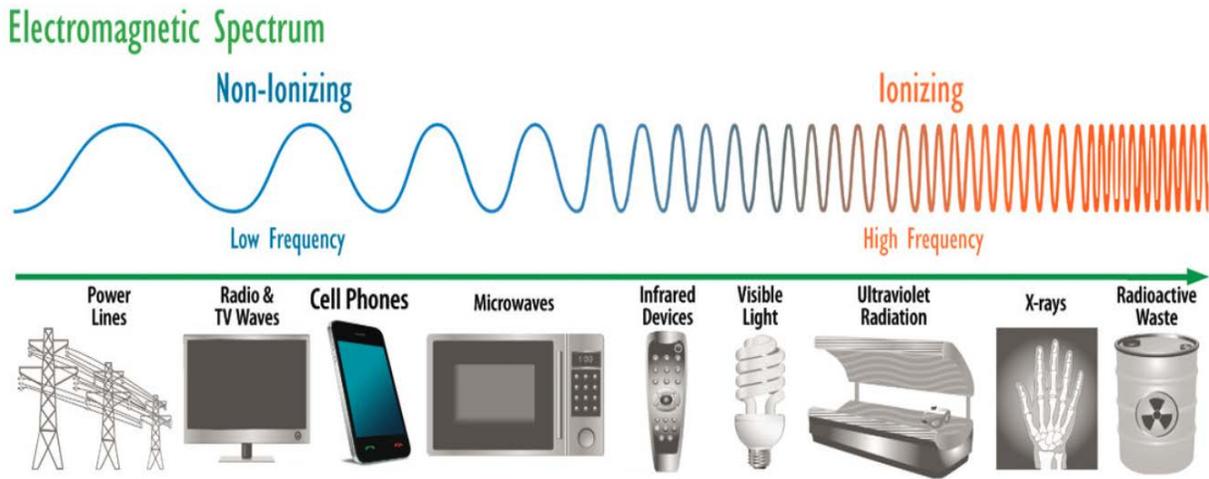
RFR used in cell phones is at the lower frequency and lower energy end of the electromagnetic spectrum.

https://www.niehs.nih.gov/health/materials/cell_phone_radiofrequency_radiation_studies_508.pdf

Figure 2.

National Toxicology Program

Headquartered at the
National Institute of Environmental
Health Sciences NIH-HHS
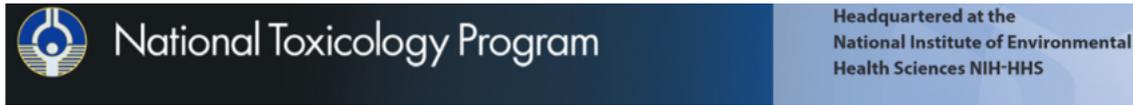
Cell Phone Radio Frequency Radiation Studies

What did the studies find?

NTP studies found that exposure to high levels of RFR, like that used in 2G and 3G cell phones, was associated with:

• **Clear evidence of tumors in the hearts of male rats.** The tumors were malignant schwannomas.

• **Some evidence of tumors in the brains of male rats.** The tumors were malignant gliomas.

• **Some evidence of tumors in the adrenal glands of male rats.** The tumors were pheochromocytomas.

For female rats, and male and female mice, it was unclear, also known as equivocal, whether cancers observed in the studies were associated with exposure to RFR.

The conclusions were based on the NTP four categories of evidence that a substance may cause cancer.

• Clear evidence (highest)
• Some evidence
• Equivocal evidence
• No evidence (lowest)

https://www.niehs.nih.gov/health/materials/cell_phone_radiofrequency_radiation_studies_508.pdf

Table 1. Long-term bioassay on 1.8 GHz base station RFR, administered at various doses to male (M) and female (F) Sprague-Dawley rats (Experiment BT 1CEMRF): results on pre-neoplastic and neoplastic lesions of the heart.[6]

Group	Dose	Animals		Hyperplasia		Endocardial		Intramural		Total	
No.	GSM-RFR			Schwann cells		Schwannoma		Schwannoma		Schwannoma	
	1.8 GHz (V/m)	Sex	No.	No.	%	No.	%	No.	%	No.	%
I	0	M	412	3	0.7	0	0.0	0	0.0	0	0.0
	(control)	F	405	2	0.5	0	0.0	4	1.0	4	1.0
		M+F	817	5	0.6	0	0.0	4	0.5	4	0.5
II	5	M	401	2	0.5	2	0.5	1	0.2	3	0.7
		F	410	0	0.0	2	0.5	7	1.7	9	2.2
		M+F	811	2	0.2	4	0.5	8	1.0	12	1.5
III	25	M	209	1	0.5	1	0.5	0	0.0	1	0.5
		F	202	0	0.0	0	0.0	1	0.5	1	0.5
		M+F	411	1	0.2	1	0.2	1	0.2	2	0.5
IV	50	M	207	5	2.4	2	1.0	1	0.5	3	1.4*
		F	202	2	1.0	1	0.5	1	0.5	2	1.0
		M+F	409	7	1.7	3	0.7	2	0.5	5	1.2

Group I: 817, male and female Sprague-Dawley rats exposed from prenatal life (12th day of mother gestation) until natural death to a 1.8 GHz GSM far field respectively of 0 V/m with a whole-body exposure for 19 h/day (control group)

Group II: 811, male and female Sprague-Dawley rats exposed from prenatal life (12th day of mother gestation) until natural death to a 1.8 GHz GSM far field respectively of 5 V/m with a whole-body exposure for 19 h/day

Group III: 411, male and female Sprague-Dawley rats exposed from prenatal life (12th day of mother gestation) until natural death to a 1.8 GHz GSM far field respectively of 25 V/m with a whole-body exposure for 19 h/day

Group IV: 409, male and female Sprague-Dawley rats exposed from prenatal life (12th day of mother gestation) until natural death to a 1.8 GHz GSM far field respectively of 50 V/m with a whole-body exposure for 19 h/day

Table 2. Long-term bioassay on 1.8 GHz base station RFR, administered at various doses to male (M) and female (F) Sprague-Dawley rats (Experiment BT 1CEMRF): results on pre-neoplastic and neoplastic lesions of the brain.[6]

Group	Dose	Animals		Meninges[a]				Glia[b]			
No.	EMF-GSM			Benign Tumors		Malignant Tumors		Glial cells hyperplasia		Malignant Tumors	
	1.8 GHz (V/m)	Sex	No.	No.	%	No.	%	No.	%	No.	%
I	0	M	412	2	0.5	1	0.2	0	0.0	0	0.0
	(control)	F	405	0	0.0	1	0.2	1	0.2	2	0.5
		M+F	817	2	0.2	2	0.2	1	0.1	2	0.2
II	5	M	401	4	1.0	4	1.0	0	0.0	3	0.7
		F	410	4	1.0	1	0.2	0	0.0	3	0.7
		M+F	811	8	1.0	5	0.6	0	0.0	6	0.7
III	25	M	209	1	0.5	1	0.5	1	0.5	2	1.0
		F	202	2	1.0	0	0.0	0	0.0	2	1.0
		M+F	411	3	0.7	1	0.2	1	0.2	4	1.0
IV	50	M	207	2	1.0	0	0.0	0	0.0	0	0.0
		F	202	2	1.0	0	0.0	0	0.0	3	1.5
		M+F	409	4	1.0	0	0.0	0	0.0	3	0.7

References

1.   IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. *Non-Ionizing Radiation, Part 2: Radiofrequency Electromagnetic Fields.* Lyon, France: International Agency for Research on Cancer;2013.

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6.   Falcioni L, Bua L, Tibaldi E, et al. Report of final results regarding brain and heart tumors in Sprague-Dawley rats exposed from prenatal life until natural death to mobile phone radiofrequency field representative of a 1.8GHz GSM base station environmental emission. *Environmental research.* 2018;165:496-503.