Radiofrequency Toolkit for Environmental Health Practitioners

BC Centre for Disease Control
An agency of the Provincial Health Services Authority

National Collaborating Centre for Environmental Health

Centre de collaboration nationale en santé environnementale

Acknowledgements

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Mona Shum has published on the assessment of exposure to wireless devices.[1-4] Richard Gallagher, formerly head of the Cancer Control Research Program at the BC Cancer Agency, researched the relationship between leukemia and children's exposure to electromagnetic fields.[5]

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Introduction to the Radiofrequency Toolkit

The Radiofrequency Toolkit was developed in response to requests from BC's medical and environmental health officers to the British Columbia Centre for Disease Control (BCCDC) for assistance in assessing and communicating the risk to health of the many devices and applications which emit radiofrequency (RF) waves. Health officers have been asked for their advice and sometimes for their involvement on issues as varied as whether children should use mobile phones, where mobile phone towers should and should not be located, whether WiFi should be allowed in schools, whether baby monitors are safe, and increasingly about the transmission strength of BC Hydro's new Smart Meters, and whether Smart Meters cause a variety of health effects.

As elsewhere, individuals and community advocacy groups in BC have expressed concerns about the widespread use of RF and about specific applications. Much of the concern is directed to wireless communication despite RF having been the basis for radio transmission since the 1920s, and despite its extensive use in health care and in industry. Information on RF and RF safety, while widely available, is often also highly technical and not easily understood.

The toolkit was a two-year project involving staff at the Environmental Health Services of BCCDC and the National Collaborating Centre for Environmental Health (NCCEH), a program funded by the Public Health Agency of Canada and housed at the BCCDC. Students, public health residents, and specialists in epidemiology from outside BCCDC collaborated with BCCDC and NCCEH staff on the project. Among contributors to the toolkit are experts in radiation physics, exposure assessment, cancer studies, and environmental epidemiology.

Intended as informative rather than definitive, the toolkit summarizes and assesses scientific research published between 2006 and 2012 on the physics, exposure, and health effects of RF. The health risk of various RF-emitting devices is put into context by offering a framework for assessing the potential strength of an RF source on the body as a function of one's distance from it, and of the frequency, continuity, and intensity of the waves that the source emits. The toolkit is based both on collections of articles assessing the RF literature and on original research articles themselves. Draft chapters were kindly reviewed by a number of public environmental health practitioners whom the toolkit was intended to serve.

Several recent international reports complement information found in the toolkit. The UK Health Protection Agency (2012) and the Norwegian Institute of Public Health (2012), among others, have published major reviews of RF and its potential effects on health; both agencies concluded that there is little evidence of adverse impacts on the health of the general population by RF. Given that some research evidence indicates the possibility of specific health effects, international organizations, including the World Health Organization, recommend ongoing research from the scientific and

regulatory communities. The BioInitiative Project (2007, revised 2012), which was produced by an international non-governmental collaborative, included epidemiological and experimental evidence, postulated biological mechanisms by which RF might cause a variety of health effects, and proposed standards for its use, far more stringent than those which Canada, among many jurisdictions, applies. In 2011, the International Agency for Research on Cancer (IARC), following extensive review of research into cancer and RF, classified RF as a *possible carcinogen*.

Somewhat different from other reviews, the toolkit incorporates sections on medical and occupational uses of RF and how they inform risk to the general public, and on measures to limit exposure.

We realize that there will continue to be divergent views of the effects of RF. And we hope that scientists from across Canada can join us in contributing their knowledge and understanding to future integrative work in this enormous field.

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March 7, 2013

Table of Contents

Section 1

Executive Summary

The toolkit was written by public health scientists and is intended as a background document, current to 2012, to assist medical health officers and environmental health officers in their role of communicating evidence of potential hazards of radiofrequency (RF) to the concerned public. RF-emitting devices such as mobile phones, baby monitors, WiFi and Smart Meters are used extensively for wireless communication, with applications also for medical and industrial purposes. Information on RF and RF safety is abundant but broadly scattered, technically complex, and not easily understood. RF emitting devices differ in such characteristics as frequency, power, and continuity of output, yet the public sometimes sees exposure to RF as a single issue without considering the strength and nature of the RF source and the distance between the source and the individual who might absorb its energy. The toolkit provides background on the physics of RF, its sources, measurement and exposure characteristics as well as an evaluation of the current scientific literature on potential biological and health effects associated with exposure to RF.

Section 2, ***Basic Physics of Radiofrequency***, examines the nature and characteristics of RF waves as part of the electromagnetic (EMF) spectrum and provides a description of modulation of RF waves (pulsed vs. continuous beams); quantities used (including power density and effective power); units of the electrical and magnetic fields, and differences in exposure according to near, intermediate, and far-field of sources.

Section 3, ***Sources of Radiofrequency Electromagnetic Fields,*** describes the variety of consumer products that emit or respond to EMF. In addition to natural and biological RF sources, RF-emitting devices include mobile phones and base stations; baby monitors; cordless phones; WiFi systems: computers, security, access points; smart meter systems; AM, FM, CB radio, TV broadcast systems; and microwave ovens. Industry sources of RF include heat sealers, induction heaters, wood gluing and radar, while medical sources include magnetic resonance imaging, ablation and tumour therapy, and short-wave diathermy.

Section.4, ***Detection and Measurement of Radiofrequency Waves,*** describes such instruments as RF detectors, receivers, survey meters and individual RF monitors. Time averaging is compared to spatial averaging with output being peak or average power. SAR measurements can be obtained by calorimetric, E-field, and graphical techniques.

Section 5, ***Assessment of Radiofrequency Exposure to the General Public***, presents data on source measurements taken in the field and in laboratories as well as personal and area measurements of multiple sources of ambient RF fields. RF emitting devices near the body are known to produce the greatest exposures (e.g., mobile phone held to the head) but once in the far-field, exposures decrease substantially. Ambient

exposures to RF are up to millions of times lower than levels from mobile phones held at the ear. Technology of the RF-emitting devices has the greatest influence on exposure levels. The original analogue mobile phone systems and the Global System for Mobile Communications (GSM) have higher energy output than newer mobile phone technologies. Environmental factors that can increase the intensity of exposure to multiple sources of RF include location (indoors vs. outdoors, urban vs. rural) and being in transit. Ongoing assessments of exposure are needed given the increasing number of sources of RF and duration of use, as well as ever-changing technology.

Section 6A, ***Biological Effects of Radiofrequency Exposure – Cell Culture Studies,*** reviews the literature on non-thermal exposure to RF and possible adverse biological effects on cells, and considers biological processes which suggest the potential for adverse health outcomes or mechanisms for health effects. There is no convincing evidence from cell culture studies that RF field exposure damages DNA (a cancer mechanism), induces cell transformation or affects a variety of physiologic processes such as calcium channelling in neurologic and other cells. Mixed or contradictory results have been found for cell proliferation, the presence of reactive oxygen species (which contain free radicals that are damaging to DNA), apoptosis (programmed cell death) in cell cultures, and changes in expression of heat shock or other genes or proteins indicative of cell stress. Overall, in spite of the many well-conducted cell culture experiments examining a number of putative effects, there is no convincing evidence that sub-thermal exposure to RF has adverse biological effects at the cellular level. On this basis, no biological mechanism proposed for such effects can be evaluated.

Section 6B, ***Biological Effects of Radiofrequency Exposure – Animal Studies***, summarizes the recent literature on the relationship between RF exposure and biological or toxicological effects in animals. Long-term bioassays, designed to determine whether RF exposure either alone or in conjunction with known mutagens can initiate or promote development of cancer in animals, have been uniformly negative. Studies of RF fields and toxicological effects such as DNA damage, micronucleus formation, apoptosis, reactive oxygen species, and gene expression changes have been inconsistent and the results have been contradictory. Positive studies have proven difficult to replicate. There is no consistent evidence that exposure to RF produces biological effects in animal central nervous systems. Recent investigations have been unable to confirm that RF exposure alters blood-brain barrier permeability; however, other aspects of brain physiology are less well studied. Behavioural investigations of the role of RF exposure on animal learning and cognitive function are mixed. Immune function studies have been mostly negative, although most of the studies to date have been conducted in adult animals. Effects of RF exposure on endocrine function, particularly on melatonin levels, have been negative, as have been studies on reproductive function in female animals. Overall, the research studies to date have not provided convincing evidence that RF-field exposure produces adverse biologic effects in animals.

Section 7, ***The Use of Electromagnetic Fields in Medicine and Its Effect on Patients and Health Care Workers***, concerns the exposure and health of patients and health care workers exposed to RF from medical devices. EMF of lower frequencies up to 200 MHz are commonly used in medicine for diagnosis and therapy, which includes exposures to RF above 100 kHz (0.1 MHz). Three main EMF applications in medicine are magnetic resonance imaging (MRI), RF ablation that destroys tumours and unhealthy tissue in heart muscle, and localized dielectric heating (short-wave diathermy) used in physiotherapy to heat surfaces or deep tissue. No long-term effects of EMF exposures to MRI patients on reproductive, cardiovascular, and cognitive function outcomes have been reported, and there is no indication of chronic effects attributed to occupational exposure to the EMF fields. Complications to patients, which may arise due to non-target thermal damage during RF ablation are usually reversible; there were no studies of occupational health risks for workers administering RF ablation. There was also no literature concerning adverse effects of dielectric heating on patients. Female physiotherapists were at a slightly increased risk for spontaneous abortions and heart disease, but these may be more related to the older practice of microwave diathermy, rather than the common use of short-wave diathermy.

Section 8, ***Health Effects Associated with Radiofrequency Exposure of Industrial Workers***, describes principal industrial uses of RF waves and assesses the literature concerning over-exposure and long-term chronic exposures of industrial workers to RF and associated health effects. Workers in a wide variety of industries are potentially exposed to higher levels of RF and for longer duration than the general population, although not necessarily at the same RF frequencies. Current safety guidelines are based on preventing the established acute effects of tissue heating and RF shock.

Industrial applications of RF include industrial microwave ovens (dryers), induction and dielectric heating, broadcasting applications (AM, FM, CB, and TV) and radar. Case reports on accidental over-exposures resulted in no long-term health effects. Brain tumours and hematopoietic cancers are the most extensively studied cancer outcomes in studies of chronic occupational RF exposure; no increased risk for any cancer site has been observed. The cardiovascular mortality studies of industrial workers also have been consistently negative.

Military personnel were the focus of many of the studies on the reproductive effects of occupational exposure to RF on semen parameters. Although there was some indication of adverse sperm effects, the studies were generally poorly done. The quality of exposure assessment and low statistical power are major limitations of observational studies. Further research into health effects associated with occupational exposures to RF is needed due to the potential for greater intensity and duration of exposure. Additionally, absorption in the body can be greater in occupational settings when lower frequency RF is used.

For **Section 9,** ***Epidemiological Studies on the Risk of Head and Neck Tumours and Cancers Associated with the Use of Mobile Phones***, long-term exposure and cancer latency are important to consider as cancer develops only after an extended period of time since first exposure. As well, the highest level of personal exposure to RF is from mobile phones held to the head. Most of the original studies cited in the reviews did not find an increased risk of head and neck tumours associated with long-term use of digital phones. However, many of the literature reviews using meta-analyses (combining study results) found increased risks of specific head tumours with longer-term use of mobile phones (typically, at least 10 years since first use), along with recall of using mobile phones preferentially at the same side of the head as the tumour.

The tumours implicated were gliomas (originating from glial cells which surround neurons and often are malignant) and benign acoustic neuromas (non-cancerous) cranial nerve tumours. No relationship was found between long-term use of mobile phones and meningiomas (tumours in tissue surrounding the brain and spinal cord) or of parotid tumours (salivary gland tumours). Because of study design issues and positive findings that have not been replicated by other researchers, doubts remain about whether exposure to RF increases the risk of brain and other cancers of the head and neck. It should, however, be noted that, based on review of the same body of evidence, the IARC Working Group review in May 2011 determined that exposure to RF from wireless phones was "possibly carcinogenic to humans (Group 2B)".

Section 10, ***Mobile Phones, Radiofrequency Waves, and Male Infertility***, provides a synthesis of research into the effects of RF from mobile phones on semen parameters and on possible mechanisms for such health effects. The epidemiological studies of men assessed for infertility were consistent in demonstrating decreased sperm motility associated with use of mobile phones. Most of the in vitro (laboratory) studies, which involved exposing human semen samples to controlled mobile phone RF exposure, generally noted a decrease in sperm motility, among other adverse effects. Similar findings were noted in animal studies of a specific type of rat. Oxidative stress or decreased antioxidants are suggested as plausible mechanisms for these non-thermal effects from RF exposure. Better exposure assessment is needed in future studies, such as determining the effect of usually carrying an active mobile phone in the front pants pocket.

Section 11, ***Neurophysiologic and Cognitive Performance Effects from Exposure to Radiofrequency Waves from Mobile Phones***, poses the question, "Is there evidence of non-cancerous effects on the brain from exposure to RF waves from mobile phones?" The conclusion from five of the most recent reviews is that cumulative evidence to date does not support exposure to RF as having adverse effects on cognitive performance, as demonstrated by current neurobehavioral tests of memory and attention. Although there is some consistency of an effect on brain activity, as indicated by enhancement of the alpha waves recorded in electroencephalography (EEG) studies, it is of unknown significance on behaviour or health. Subtle effects on

brain physiology may be better characterized with new types of neurophysiologic techniques, such as measurement of brain glucose metabolism, and carefully designed replicable larger-scale studies. Whether effects on brain activity or physiology translate to adverse behavioural or health effects remains unclear.

Section 12, ***Symptoms Attributed to Radiofrequency / Electromagnetic Fields***, assesses observational studies and experimental (provocation) studies to determine the association of non-specific symptoms with exposure to RF for the general public and to electrohypersensitive (EHS) individuals who attribute their health effects to exposure to electromagnetic fields, including RF. Findings from population health studies of exposures from mobile phones and mobile phone base stations are mixed and inconsistent and are prone to study design issues including poor exposure ascertainment. The prevalence of EHS is estimated to vary from 1% to 10% of the population. In general, subjects who are self-declared with "EHS" do not reliably detect RF when blinded to the source, and RF fails to trigger symptoms in self-declared EHS individuals in a reliable, reproducible, and consistent way. However, provocation studies are limited to examining acute (short-term) exposure to RF, and acute symptoms and the effects of cumulative, chronic exposure to RF on persistent human health symptoms have not been studied thoroughly.

Section 13, ***Radiofrequency Safety Guidelines and Standards***, provides an overview and commentary on Safety Code 6 – Health Canada's radiofrequency exposure guidelines, with comparison to the internationally recognized guidelines by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) and to exposure limits used in other countries. The main basis for regulation is to prevent thermal effects due to the absorption of RF by soft tissue. The RF exposure limits for the general public in Canada, like the USA and Japan, are slightly higher at 6 W/m^2 than the ICNIRP standard (4.5 W/m^2) for frequencies of 900 MHz (e.g., GSM mobile phones and base stations, and some Smart Meters). Whether and how the much lower limits of 0.10 W/m^2 for Eastern European countries are enforced is not known.

Section 14, ***Strategies for Radiofrequency Exposure Reduction,*** offers an occupational hygiene approach for the option of minimizing personal exposure to RF. This includes: 1) substitution, by replacing wireless RF devices such as phones with hard-wired alternatives; 2) engineering controls through modifications such as power-saving or non-idling functions; 3) administrative controls including limiting duration and frequency of use as well as distancing (e.g., use headsets, speaker phone, or text-messaging for mobile phones). Shielding from RF by adding mobile phone shields or wearing protective devices such as metallic clothing or headgear has limited effectiveness and may even increase exposure to RF.

Section 15, ***Overview of Major Ongoing Research Projects on Electromagnetic Fields and Health***, provides a description of six international research projects on EMF and health: 1) The EMF project of the World Health Organization (WHO); 2) MOBI-KIDS

project: Study on Communication Technology, Environment and Brain Tumours in Young People; 3) EFHRAN: European Health Risk Assessment Network on Electromagnetic Fields Exposure; 4) COSMOS project: Cohort Study of Mobile Phone Use and Health; 5) Sound Exposure & Risk Assessment of Wireless Network Devices (SEAWIND); and 6) National Toxicology Program (NTP) Rodent project.

Section 16, *International Reports on Radiofrequency Exposures and Health Effects*, describes the content of recent reports reviewing biological and health effects associated with exposure to RF and EMF. These included: 1) AGNIR, the Advisory Group on Non-Ionizing Radiation (UK); 2) the BioInitiative report; 3) EFHRAN, the European Health Risk Assessment Network; 4) ICNIRP, International Commission on Non-Ionizing Radiation Protection; 5) Latin American Experts Committee on High Frequency Electromagnetic Fields and Human Health; 6) Norwegian Institute of Health Expert Committee, Report 2012; 7) SCENIHR, Scientific Committee on Emerging and Newly Identified Health Risks; and 8) the Swedish Radiation Safety Authority - SSM:s Independent Expert Group on Electromagnetic Fields.

Section 2

Basic Physics of Radiofrequency

Table of Contents

2.1 Symbols and Units

E Electric field, in units of Volts per meter (V/m)

H Magnetic field strength in units of Ampere per meter (A/m)

B Magnetic flux density in units of Tesla (SI) or Gauss (CGS)

f Frequency of a wave, in units of Hertz (Hz)

λ Wavelength of a wave, in meters (m)

A Ampere, unit of electric current

V Volt, unit of electric voltage

T Tesla, SI unit of magnetic flux density

G Gauss, CGS unit of magnetic flux density

W Watt, unit for electric power

S Power density, in units of Watts/m^2

m Meter, unit for distance

dB Decibel, logarithmic unit (dimensionless)

dBm Decibel-milliWatt, logarithmic unit (dimensionless)

dBW Decibel-Watt, logarithmic unit (dimensionless)

dBi Gain of an antenna relative to an isotropic RF source (dimensionless)

Ω Ohm, electrical unit of resistance

2.2 Useful Definitions

2.2.1 Electromagnetic (EM) radiation

EM radiation is the energy transmitted through space in wave form, which can be characterized in terms of a wavelength **λ** or a frequency **f**.

2.2.2 RF antenna

An antenna is a device used to emit and receive radiofrequency (RF) waves. As an emitter, it transforms high frequency signals traveling on a conductor into electromagnetic (EM) waves in free space.

2.2.3 Radiofrequency

Radiofrequency is a frequency within the electromagnetic spectrum used for radio transmission. For purposes of this toolkit, the frequency range of interest is 100 kHz to 300 GHz, as shown in Table 1.[1]

Table 1. Frequency band designations

FREQUENCY	BAND CODE	BAND DESCRIPTION
30 Hz-300 Hz	SLF	Super Low Frequency
300 Hz-3000 Hz	ULF	Ultra Low Frequency
3 kHz-30 kHz	VLF	Very Low Frequency
30 kHz-300 kHz	LF	Low Frequency
300 kHz-3 MHz	MF	Medium Frequency
3 MHz-30 MHz	HF	High Frequency
30 MHz-300 MHz	VHF	Very High Frequency
300 MHz-3 GHz	UHF	Ultra High Frequency
3 GHz-30 GHz	SHF	Super High Frequency
30 GHz-300 GHz	EHF	Extremely High Frequency

2.2.4 Wavelength of RF waves

Distance covered by one complete cycle of the RF wave, as shown in Figure 1.

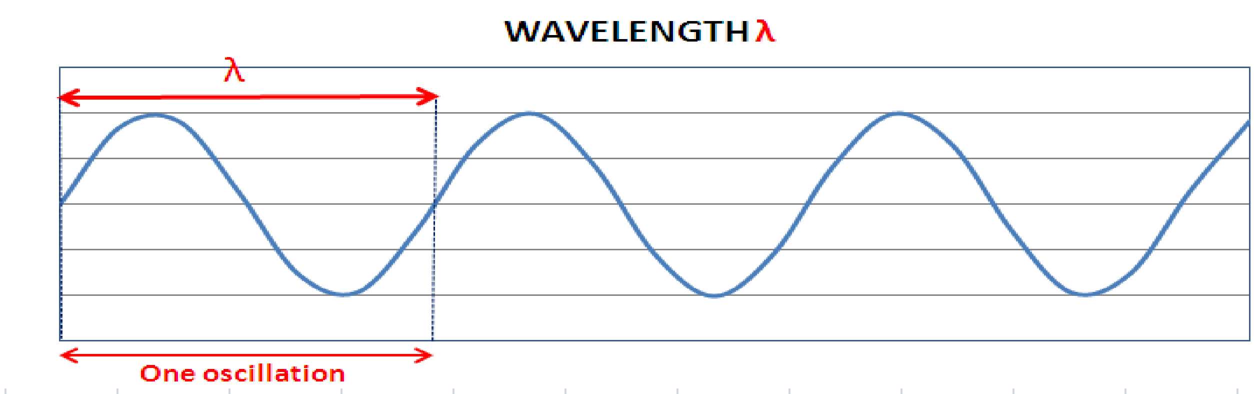


Figure 1. Wave Characteristics

2.2.5 Frequency of RF waves

Frequency of RF waves is the number of EM waves passing a given point in one second. The frequency is expressed in Hertz (Hz).

2.2.6 Bandwidth of an RF antenna

The bandwidth of an antenna refers to the range of frequencies over which the antenna operates correctly.

2.2.7 Power density

Power density is the power per unit area perpendicular to the direction of propagation, usually expressed in terms of Watts per square meter (W/m^2) or milliWatts per centimeter-squared (mW/cm^2).

2.2.8 Decibel (dB)

A decibel is a measure of the increase or decrease in power, P, at two points 1 and 2 expressed in logarithmic form:

$$\text{Power Ratio in dB} = 10\text{Log}\left(\frac{P_1}{P_2}\right) \qquad \textit{(2.1)}$$

- *Decibel-milliwatt (dBm)*:

Electrical power unit in decibels referenced to 1milliWatt (mW), as expressed below:

$$P(\text{dBm}) = 10\text{Log}\left[\frac{P(\text{mW})}{1\ \text{mW}}\right] \qquad \textit{(2.2)}$$

- *Decibel-Watt (dBW)*:

Electrical power unit in decibels referenced to 1Watt (W), as expressed below:

$$P(\text{dBW}) = 10\text{Log}\left[\frac{P(\text{W})}{1\ \text{W}}\right] \qquad \textit{(2.3)}$$

2.2.9 Antenna gain/loss in dBi

This is the antenna's gain or loss G over a theoretical **isotropic** antenna (radiating evenly in all directions).

$$Gain\ G\ (dB) = 10Log\left(\frac{P_1}{P_2}\right) \qquad (2.4)$$

Where:

- P_1 is the power from the antenna at a point X in space.
- P_2 is the power from a hypothetical isotropic radiator at the same point X.

Example:

If an antenna has a gain G of 6 dBi in a certain direction, it means that the power of the transmitter is multiplied by 4, as shown below:

$$\frac{P_1}{P_2} = Inv\ [Log_{10}\left(\frac{6}{10}\right)] = 10^{0.6} = 4 \qquad \textit{(2.5)}$$

2.2.10 Equivalent isotropically radiated power (EIRP)

The equivalent isotropic radiated power (EIRP) is defined as the product of the power supplied to the antenna $\mathbf{P_t}$ and the antenna gain $\mathbf{G_t}$, both quantities expressed in linear terms (not in decibels):

$$\mathbf{EIRP\ (W) = P_t\ \ (W) \,.\, G_t} \qquad \textit{(2.6)}$$

It is the power that would be radiated by an isotropic source if it had an input power equal to $\mathbf{P_t}$ $\mathbf{G_t}$.

In equation *(2.6)*, **EIRP** and $\mathbf{P_t}$ are expressed in units of Watt while $\mathbf{G_t}$ is dimensionless.

In decibels (dimensionless), EIRP is equal to the sum of $\mathbf{P_t}$ (dBW) and $\mathbf{G_t}$ (dBi):

$$\mathbf{EIRP(dBW) = P_t(dBW) + G_t(dBi)} \quad (2.7)$$

Example:

Suppose $\mathbf{P_t}$ = 20 Watt and the antenna Gain $\mathbf{G_t}$=5

- In units of Watt, EIRP is equal to: **20 W x 5 = 100 W**
- In units of decibel-power (dimensionless):

$\mathbf{P_t}$ (dBw) = 10 Log (20) = 13.01

$\mathbf{G_t}$ (dBi) = 10 Log (5) = 6.99

Therefore: $\mathbf{EIRP}\ (\mathbf{dBW}) = \mathbf{10\ Log}\ (\mathbf{20}) + \mathbf{10\ Log}\ (\mathbf{5}) = \mathbf{13.01} + \mathbf{6.99} = \mathbf{20}$ dBw *(2.8)*

Note: In equations *(2.6)* and *(2.7)*, signal losses in cables are assumed negligible.

2.2.11 Continuous RF wave (CW)

A continuous radiofrequency wave is a RF signal that is not altered by modulation. It is therefore is described by a constant frequency, constant amplitude, and steadily advancing phase. In other words, continuous waves are successive oscillations which are identical under steady-state conditions.

2.2.12 Modulation of RF waves

Wave modulation occurs when some characteristic of the wave is varied.

a. Pulse modulation:

In pulse modulation, pulsed waves are emitted in short pulses, i.e., RF energy is rapidly switched ON and OFF, as shown in Figure 2.

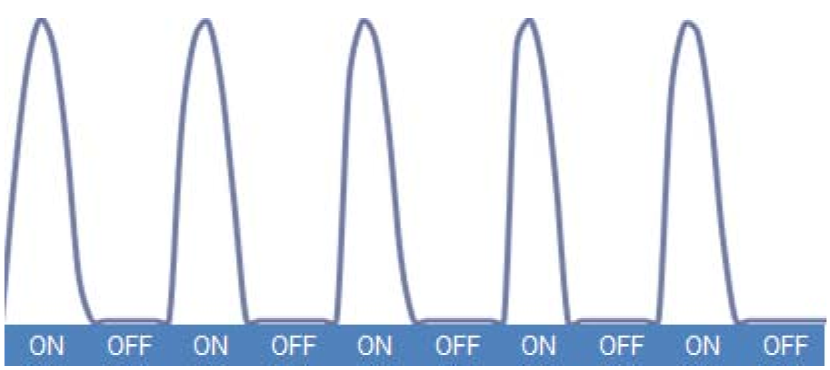


Figure 2. Pulsed waves

For example, Global System for Mobile Communications (GSM) technology uses eight slots. The assignment of one slot per user gives rise to the pulsed nature of the wave; a GSM phone will only be transmitting 1/8th of the time, i.e., 1/8th duty cycle.[2]

Other examples: keyless entry, pulsed NMR systems, analog or digital radar for airports, ships, speed detection, military, satellites, electronic test equipment.

b. Amplitude modulation:

RF waves are continuously emitted with changing energy (amplitude), as shown in Figure 3.

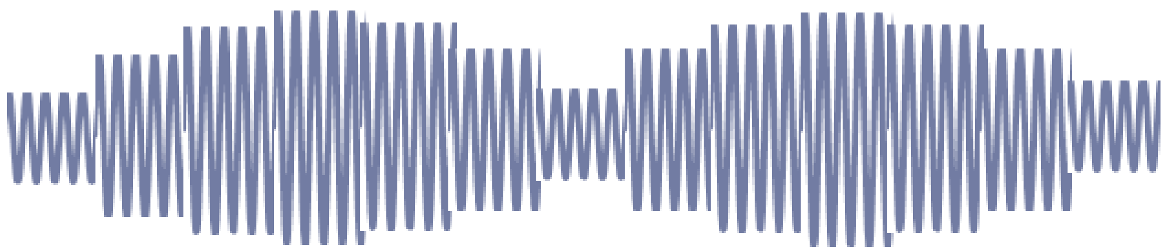


Figure 3. Amplitude-modulated waves

Examples of amplitude modulation: AM radio, amateur radio.

c. Frequency modulation:

RF waves have constant amplitude with change of frequency in small amounts, as shown in Figure 4.

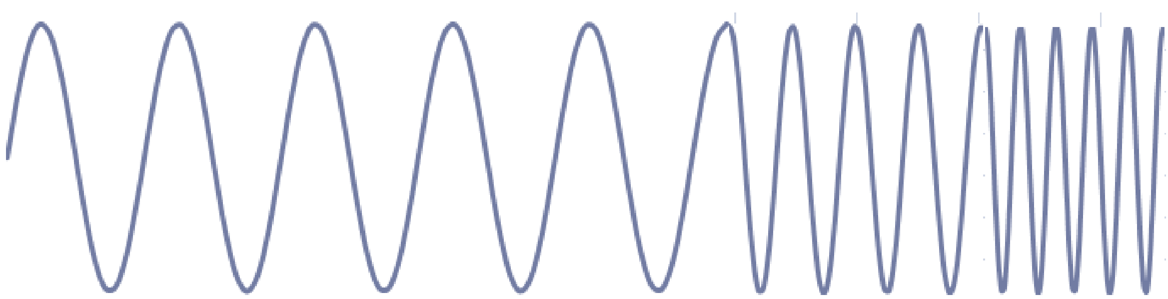


Figure 4. Frequency-modulated waves

Examples of frequency modulation: FM radio, amateur radio, data and fax modems, telemetry, radar, seismic prospecting and newborn EEG seizure monitoring[3]:

2.2.13 Electric field

The region surrounding an electric charge, in which the magnitude and direction of the force on a hypothetical test charge is defined at any point. The electric field produces a force on electrically charged objects.

Electric field strength E:

The magnitude of the electric field vector (in units of Volts/meter, V/m)

Magnetic field:

A force field associated with changing electric fields (when electric charges are in motion). Magnetic fields exert deflective forces on moving electric charges.

A magnetic field can be specified in two ways: as magnetic flux density B or magnetic field strength H.

Magnetic flux density B:

B is the amount of magnetic flux through a unit area taken perpendicular to the direction of the magnetic flux, in SI units of Tesla (T) or CGS units of Gauss (G).

$$1 \text{ Gauss} = 10^{-4}\text{Tesla} = 100\mu\text{Tesla} \quad (2.9)$$

Magnetic field strength H:

H is the magnitude of the magnetic field vector (in units of Amperes/meter, **A/m**)

Relation between B and H:

The two quantities are related by the expression:

$$B = \mu H \quad (2.10)$$

Where μ is the magnetic permeability. In a vacuum and in air, as well as in non-magnetic (including biological) materials, μ has the value $4\pi\ 10^{-7}$ expressed in units of Henry per meter ($H.m^{-1}$). Therefore, a magnetic field can be described by either of the two quantities, B or H.

2.2.14 Power density in the far field

The power density S is the product of the electric field E and the magnetic field H:

$$S = E.H \quad (2.11)$$

In the far field, an estimate of the RF power density can be determined by means of the following equation[1]:

$$S = \frac{P_t\, G_{max} \delta\, \gamma}{4\pi R^2} \quad (2.12)$$

Where:

- S is the power density ($Watt/m^2$)
- P_t is the power of the transmitter (Watt)
- G_{max} the maximum Gain of the antenna (dimensionless)

- δ the duty cycle of the RF source (dimensionless)
- γ a factor that accounts for possible ground reflections (dimensionless)
- R the distance from the RF source (meters)

2.2.15 Root- mean- square (rms) Electric (E) and magnetic (H) fields

This is the square root of the average of the squares of the instantaneous **E field** or **H field** taken over a time interval.

For example, if n values E1, E2, … En of the electric field are recorded during an interval of time, the rms electric field current is calculated as follows:

$$rms\ E = \sqrt{\frac{1}{n}(E_1^2 + E_2^2 + E_3^2 + \cdots E_n^2)} \qquad \textbf{(2.13)}$$

Similarly, the rms magnetic field is:

$$rms\ H = \sqrt{\frac{1}{n}(H_1^2 + H_2^2 + H_3^2 + \cdots H_n^2)} \qquad \textbf{(2.14)}$$

2.3 General Properties of RF Waves[4]

RF waves are EM waves that:

- can be found in nature or be man-made
- propagate in free air and dense media. Their propagation obeys the inverse square law at sufficient distance from the antenna (far field).
- travel at the speed of light (300,000 Km/second)
- carry energy as they propagate
- can transfer their energy to matter
- can be used to carry information
- can be broadcast outwards to reach many locations or can be formed into beams to reach a particular spot
- can be reflected or refracted when interacting with a dense medium
- can travel great distances
- travel in straight lines
- can pass through walls
- can be captured by placing a metal rod, a loop, parabolic metal dish, or horn in its path.

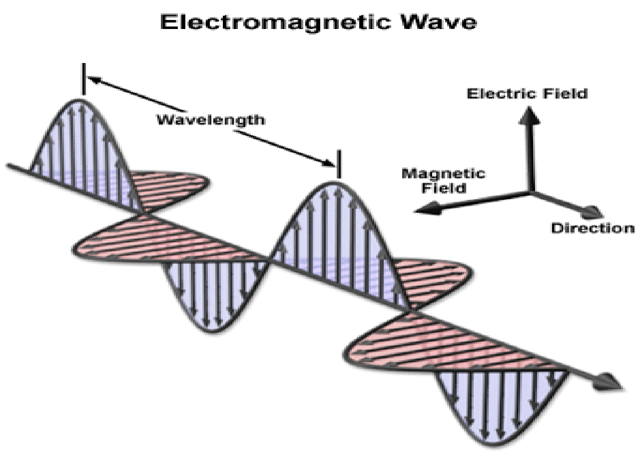
2.4 RF Fields

The electromagnetic field is composed of an electric field E and a magnetic field H. They both produce forces on electric charges.

Static electrical charges produce an electric field while charges in motion produce a magnetic field.

A changing magnetic field can move electric charges to induce currents in its interaction with a medium.

An RF wave is a moving electromagnetic field that has velocity in the direction of travel and components of electric field E and magnetic field H arranged at right angles to each other (Figure 5). The RF field transmits and receives RF energy through free space.

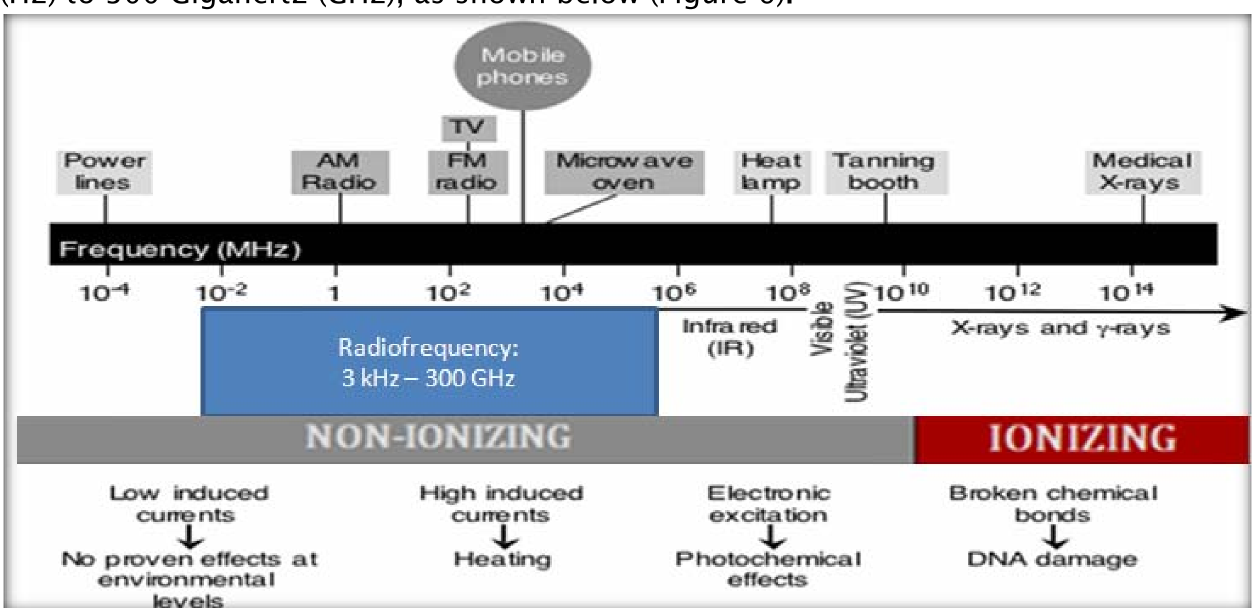


"Electromagnetic wave", used for educational and research purposes, courtesy of Magnet Lab, Florida State University

Figure 5. Schematic representation of the propagation of RF waves

2.5 RF Waves in the Electromagnetic Spectrum

RF waves are part of the electromagnetic spectrum in the frequency range of 300 Hertz (Hz) to 300 Gigahertz (GHz), as shown below (Figure 6).



Adapted from: Foster and Moulder (2000).[5]

Figure 6. Non-ionizing fields spectrum

2.6 Characteristics of RF Fields

EM waves have a wavelength and a frequency related by:

$$\lambda = \frac{c}{f} \quad \textit{2.15)}$$

Where:

- c is the velocity of light = 3 10^{8} m/s= 300,000 Kilometers per second (km/s)
- f is the frequency in Hertz (or sec^{-1})
- λ is the wavelength in meters (m)

RF waves can propagate through various media, particularly air. Their propagation characteristics depend on their frequency f (or wavelength λ) but also on the physical properties of the absorbing media. The speed of an RF wave in a vacuum is equal to the speed of light.

RF emitters transmit their signals in either Continuous Wave (CW) mode or Pulsed Wave (PW) mode.

In a CW mode, the waves are emitted in a continuous command. The power output of a continuous system is expressed in terms of average power.

In a PW mode, the waves are emitted in short pulses repeated at regular intervals. The output of a pulsed system is expressed in terms of peak power. The average power for a pulsed system is:

$$P_{avg} = D_c P_{max} \quad \textit{(2.16)}$$

Where:

- P_{avg} is the average power in Watts (W)
- D_c is the duty cycle (dimensionless)
- P_{max} is the peak power in Watts (W)

2.7 Production of RF: RF Antennas

RF fields are produced by RF antennas. The role an RF antenna is to focus and intensify the initially generated waves. Two types of antennas are usually used for the production of RF: stationary antennas and rotating antennas.

2.7.1 Stationary antennas

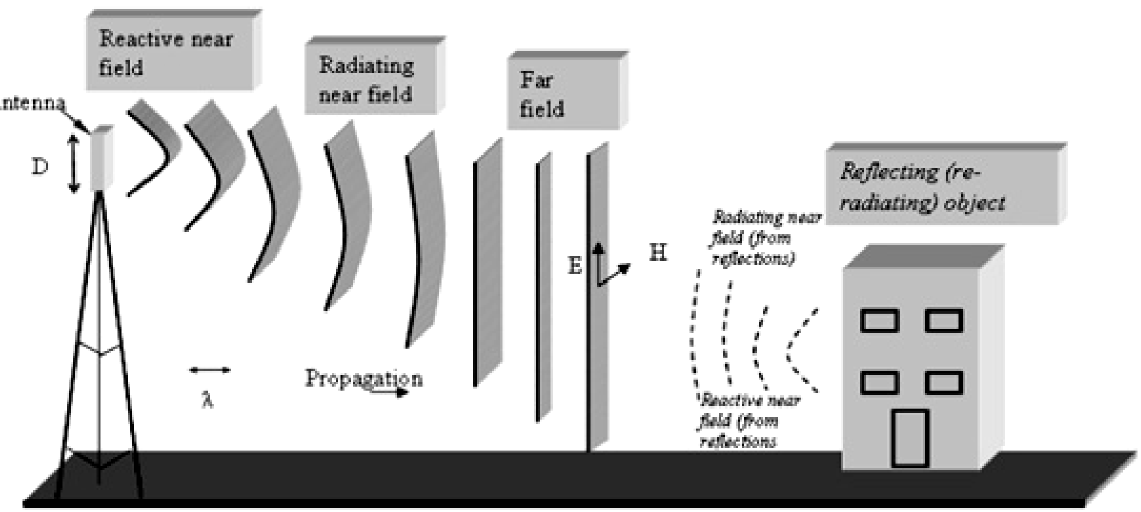
Stationary antennas are fixed antennas. They are widely used for radio broadcasting, mobile phones and base stations, FM radios, Wifi systems, cordless phones, GPS, etc. The size of the antenna is much larger than the wavelength λ of the emitted waves.

The antenna focuses the original RF signal into narrow and intense RF beams. The focusing potential of the antenna is quantified by its Gain G which is a measure of the proportion of the input power that is concentrated in a particular direction.

The RF waves generated by an antenna have different properties at varying distances from the RF source.

Three regions are commonly considered in the path of RF fields (Figure 7):

- The Near Field (nf)
- The Intermediate Field (if) also known as the Fresnel region
- The Far Field (ff) also known as the Fraunhofer region



"Near, Intermediate, and Far Fields", used for educational and research purposes, courtesy of International Commission on Non-Ionizing Radiation Protection (2009).[7]

Figure 7. Propagation of RF waves

2.7.1.1 The near field

The near field is the EMF that exists at the RF source and extends to a distance of one wavelength from the antenna.

In this region where the phase differences between waves emitted at different points of the antenna are relatively large, the relationship between the Electric Field E and the Magnetic Field H is not well defined.

The near field is divided into two sub-regions:

- The reactive near field where the strength decreases rapidly with distance from the antenna
- The radiating near field where the average power density remains fairly constant at different distances from the antenna, with some localized fluctuations.

The ideal radiating near field conditions occur at a distance D_{nf} from the antenna on the order of:

$$D_{nf} = \frac{\lambda}{2\pi} \qquad (2.17)$$

Where λ is the wavelength of the RF wave.

For example if the frequency of the RF wave is 900 MHz (i.e., λ=33 cm), the distance D_{nf} is about 5 cm.

It is assumed that the near field extends to a distance of the order of one wavelength λ. In the case of a 900 MHz wave, the near field would extend to a maximum distance of 33 cm from the antenna.

For large antennas with a dimension D (diameter or largest dimension of the antenna) larger than one wavelength, the radiating near field region extends from:

$$\frac{\lambda}{2\pi} \ to \ 0.5\frac{D^2}{\lambda} \qquad (2.18)$$

Regarding the power density of the RF waves in the near field and because of the phase differences, it is practical to consider that the peak power density all the way through the near field is four times the average power density of the antenna S_0, as follows:

$$S_{nf} = 4S_{0=}\frac{4P}{A} \qquad (2.19)$$

Where:

- P is the power output of the antenna (Watt)
- A is the area of the antenna (m^2)

In the near field region, it is useful to measure the electric field E (in Volts per meter) and the magnetic field H (in Amperes per meter) and compare the values to the Limits of Canada Safety Code 6.

The quantities E and H are related as follows:

$$Z = \frac{E}{H} \qquad (2.20)$$

Where Z is the impedance in air, in units of Ohms (Ω).

The value of the impedance Z is <u>not constant in the near field</u>. It could be lower than 377 Ohms if the predominant field is magnetic and larger than 377 Ohms if the predominant field is electric.

2.7.1.2 The intermediate field

It starts after the near field and ends before the start of the far field. In this region, because of the phase differences between waves, the RF power density alternates between maximum and minimum levels in a similar way to the near field. Therefore, the power density in the intermediate field also follows Equation ***(2.20)***.

The intermediate field extends from 0.5 D^2/λ to $2D^2/\lambda$ where D is the largest linear aperture dimension of the antenna and λ the wavelength of the wave.

2.7.1.3 The far field

The far field is the electromagnetic field located beyond the near field. It starts at a distance D_{ff} from the antenna defined as follows:

$$D_{ff} = \frac{2D^2}{\lambda} \qquad (2.21)$$

(Note that in Canada Safety Code 6 it is recommended taking D_{ff} as $0.5D^2/\lambda$ meaning that the intermediate field could be considered part of the far field).

In the far field, the electric field E and the magnetic field H are orthogonal and the free space impedance is equal to **377 Ω**. Therefore, the relation between E and H in the far field is:

$$Z_0 = \frac{E}{H} = 377 \qquad (2.22)$$

Consequently, the power density in the far field is equal to:

$$S = E.H = \frac{E^2}{377} = 377H^2 \qquad (2.23)$$

In the far field, the measurement of only one quantity, E or H or S, is enough. The other quantities can be calculated by means of equation ***(2.23)***.

2.7.2 Rotating antennas

Rotating antennas transmit RF waves in a given direction part of the time. This type of antennas is usually used for search and detection purposes, e.g., radars.

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Section 3

Sources of Radiofrequency Electromagnetic Fields

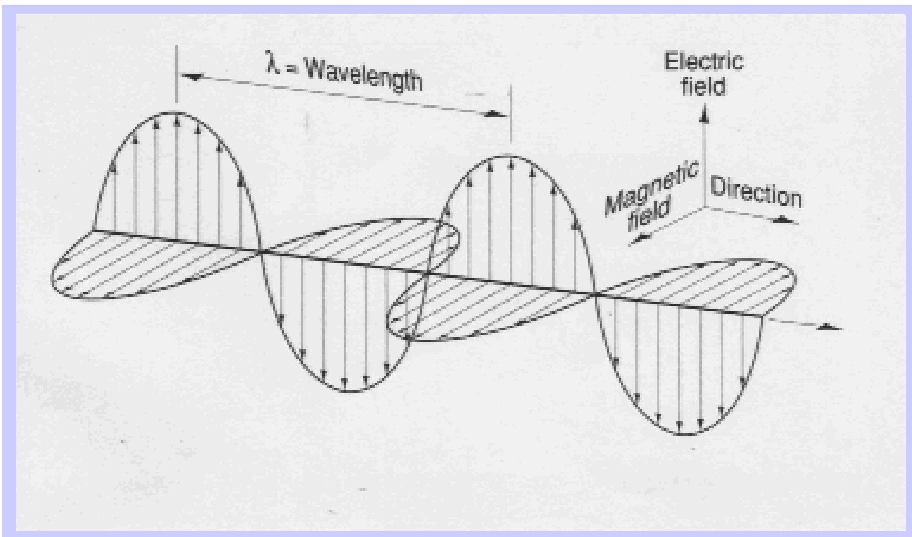
Table of Contents

3.1 Radiofrequency Electromagnetic Waves

What Is a Radiofrequency (RF) Wave?

RF waves are electromagnetic (EM) waves used for radio transmission. They carry electromagnetic energy as they propagate in free air and dense media.

A changing electric field will create a changing magnetic field, and a changing magnetic field will create a changing electric field.[1]



"TEM wave" courtesy of Wikibooks (CC BY-SA)

What Is a Continuous RF Wave?

RF wave(s) with:

- successive identical oscillations
- constant height (amplitude)
- constant repetition (frequency)
- constant output power equal to the average power
- varying sinusoidally with time.[2,3]

Examples: power supplies, plasma etching, welding/cutting arcs, continuous wave NMR, antennas, mobile phone communication, cordless phones, AM and FM broadcasting, anti-theft devices, RF heat sealers, portable radio systems, burglar alarms, microwave ovens, etc.

What Is a Pulsed RF Wave?

RF waves that are pulsed:

- The transmitter is pulsed, i.e., “on” for a short time and turned “off” for a longer time.
- Best example: radar
- Common radar frequencies: 50–330 MHz, 300–1,000 MHz, 1–2 GHz, 2–4 GHz, 4–8 GHz, 8–12 GHz, 12–18 GHz, 18–27 GHz, 27–40 GHz, 40–100+ GHz[4,5]
- Human exposures to radar systems are from police speed control radar, airplane and ship radar, meteorological precipitation monitoring, and ground-penetrating radar for geological observations.
- Examples of pulsed RF devices: keyless entry pulsed NMR systems, analog or digital radar from airports, ships, speed detection, military devices, satellites, electronic test equipment, etc.

What is the “microwave hearing effect”?

An ability of some people with normal hearing to perceive pulsed RF fields.[6]

Natural Sources of RF

Natural RF emitters:

- earth
- sun
- thunderstorm activity
- the ionosphere
- deep-space extraterrestrial sources

Thunderstorm RF:

- 30–300 MHz
- Very High Frequency (VHF)[7-9]

Characteristics of Natural RF:

- Does not pass through hills or large structures
- Cannot be transmitted beyond the horizon
- Does not bend readily around the earth's curvature
- Is reflected from the atmosphere.

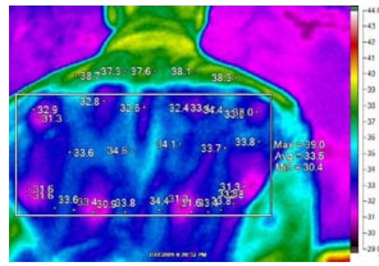
RF Utility: Little use has been made of naturally generated VHF fields.

Biological Sources of RF/EMF

Humans and mammals emit EMF energy

A human body, at 37˚C, emits an EMF of:

- Frequency: 31 THz *(31,000 GHz)*
- Wavelength: 9.66 µm



"Thermal image" courtesy of Dhama InnovationsPvt. Ltd., Wikimedia (CC BY-SA)

3.2 Consumer Products

Wireless Phone Evolution

First generation (1G) mobile phones – 1980s[10]

- Frequency: 450 MHz, 800-900 MHz
- Radiated power: 600 mW (0.6 W)
- Analogue circuit-switched technology

"History of mobile phones" courtesy of Marus, Wikipedia (CC BY-SA)

Second generation (2G) mobile phone systems – 1990s

- Frequency: 800, 900, 1500, 1800, 1900 MHz (US)
- Pure digital technology
- Caller identity and text messaging

"Cell Phone Cameras" courtesy of compujeramey, Flickr (CC BY)

Third generation (3G) mobile phone systems – 2001

"Mobile phone" courtesy of Irfan Nasir, Wikipedia (CC BY-SA)

- Frequencies: 1885–2025, 2110–2200 MHz
- Added broadband internet and high-tech video calls
- Able to use 2G and 2.5G networks where the 3G service unavailable[11]

Wireless Phones

- Frequencies: 850 MHz, 900 MHz, 1700 MHz, 1800 MHz, 1900 MHz, 2100 MHz
- Power emitted: maximum power transmitted 1 to 2 watts
- RF exposure is below HC SC 6 when radiating structure is 2.5 cm away from body
- RF exposure: When **less than** 2.5 cm from the body (excluding hands, wrists, feet, and ankles), the potential for exceeding Specific Absorption Rate (SAR) limit depends on the operating configurations and exposure conditions of the device
- Phones emit **less power** when close to base station.[12]

"charade #47 answer" courtesy of ndrwfgg, Flickr (CC BY)

Mobile Phone Base Stations

- Emit less RF than non-cable television transmitter
- Are low-power, multi-channel, two-way radios
- Antennae transmit ~ 60 watts of RF power
- Public exposures **at several meters from antennae** are typically **3000 to 1,000,000 times below HC SC 6**
- Dead zones occur when handset or mobile site is blocked by hilly terrain, excessive foliage, physical distance, or excessive cell phone use[13-16]

Baby Monitors

"Baby Monitor" courtesy of Jpsammy, Wikipedia (CC BY-SA)

- Frequencies: 16 MHz, 9.3–49.9 MHz, 900 MHz, 2.4 GHz
- Range: up to 300 m[17,18]
- Power: 0.010 W to 3 W

Bluetooth Devices

- Frequencies: 2.4 to 2.485 GHz – Industrial, Scientific and Medical (ISM) band
- No license required
- Range: short range of 5-100 m
- Power at head: 100 mW[19]
- Bluetooth products: Over 500 products including hands-free calling, GPS navigation, portable music players, wireless headsets, wireless speakers, wireless hands-free car systems, printers, laptops, cameras, health and fitness device computers, heart rate monitors, phones, home security systems, etc.

"Bluetooth Earbud" courtesy of topgold, Flickr (CC BY)

DECT, Digital Enhanced Cordless Telecommunication

- Frequencies: 902-928 MHz, 1880-1900 MHz, 1920-1930 MHz
- Range: 91 m in open area[20-22]

Cordless Phones

- Frequency: 43-49 MHz, 900 MHz, 2.4 GHz and 5.8 GHz
- Range: 12-75 m, 20-200 m, 60-450 m, 90-600 m
- Long Range: Up to 10 km
- Power: 1-5 watts[23]
- Emitted Power: 0.2-1.0 mW/cm^2
- Older cordless phone constant power: 10 mW
- Digital cordless phones – millisecond transmissions, average power: 0.01 mW

"Cordless Phone" courtesy of JDB Photos, Flickr(CC BY-NC-SA)

Wireless Head Phones

- Frequency: 86-108 MHz, 863 MHz, 900 MHz, 913.5 MHz, 914 MHz, 914.5 MHz, 925 MHz, 926.0 MHz, 926.5 MHz, 2.4 GHz
- Range:
    - Home use: 1-3 m, 3-9 m, 10 m +
    - Industrial: 6-100 m[24]

Uses: listening to music, watching a video

"Wireless Stereo Headset H3070" courtesy of audiovisualjunkie, Flickr (CC BY-NC-ND)

Wireless Home Security

- Frequencies: 43–49 MHz, 433 MHz, 902–928 MHz, 2.4 GHz–2.4835 GHz, 5.725 GHz and 5.850 GHz
- Typical output power: 10 to 100 mW (0.01–0.1 watts)
- RF emissions: 0.1% of HC SC 6 allowable exposure limits[25]

Wi- Fi Systems

- Frequency: 2.4 GHz, 915 MHz, 5.8 GHz
- Power density: <0.003 W/m^2 to 0.03 W/m^2
- Typical exposures: 1.8–4.6 V/m
- HC SC6 exposure limit: typical exposures 0.03% to 0.3% of HC SC6 limits
- Health Protection Agency: typical exposure 100 mW (0.1 W)[26-30]

Smart Meters

- Frequency: 902–928 MHz
- End point power: ¼ Watt or 0.25 W
- Maximum power (cell relays): <0.5 W
- Instantaneous power density: at 30 cm: 0.02 to 0.04 W/m^2 (2 to 4 μW/cm^2)
- Typical accumulated emission duration: approximately 60 seconds per day
- RF emissions from Smart Meters[31,32]: Far below HC SC 6 exposure limits at 900 MHz: 600 μW/cm^2

Example of measured instantaneous peak power densities from Smart Meters:

- One Smart Meter at 30 cm–3.2 μW/cm^2
- One Smart Meter at 1 m–2.0 μW/cm^2
- One Smart Meter at 3 m–1.2 μW/cm^2
- Ten operating Smart Meters at 30 cm–4.0 μW/cm^2

  Ten operating Smart Meters at 1 m–2.6 μW/cm^2

  Ten operating Smart Meters at 3 m–1.8 μW/cm^2

“Smart Meter” courtesy of Duke Energy, Flickr (CC BY-NC-ND)

Source: http://www.bccdc.ca/NR/rdonlyres/43EF885D-8211-4BCF-8FA9-0B34076CE364/0/452012AmendedReportonBCHydroSmartMeterMeasurements.pdf

AM Radio, FM Radio, and TV Transmissions

- Amplitude modulation (AM) radio frequency: 550 to 1600 kHz
- Frequency modulated (FM) radio frequency: 88 to 108 MHz
- Airborne television (TV) transmission frequency: 300 to 400 MHz

  o Humans absorb up to five times more RF from FM radio and TV than from mobile phone base stations[33]

  o SC 6 exposure limits exceeded 1–2 m from AM radio antennae

  o SC 6 exposure limits exceeded 1–2 m from FM radio antennae

  o High powers present danger of electrocution with contact[34]

  o WorkSafeBC regulates permissible exposures to workers[35]

(left) "Superturnstile Antenna" courtesy of Hans-Peter Scholz, Wikipedia (CC BY-SA)

(middle) "ENOME Anywhere!" courtesy of Coolmitch, Flickr (CC BY-NC-ND)

(right) "broadcast antenna" courtesy of HerPhotographer, Flickr (CC BY-NC-SA)

CB and FRS Radio

- Frequency: CB – 27 MHz, Family Radio Service (FRS) – 462/467 MHz
- Power: CB: 4 W; FRS: 500 mW–2 W[36]

"Amateur Radio Rig" courtesy of Joshua Fuller, Flickr (CC BY-NC)

Microwave Ovens

"Microwave" courtesy of DerekL, Flickr (CC BY-NC-SA)

- Frequency: home 2.45 GHz; industrial 915 MHz
- Power: home 400–1400 W
  - o Typical microwave oven leakage: up to 1 mW/cm^2
  - o Average microwave oven leakage 0.17–0.52 mW/cm^2[37,38]
  - o Physical/structural damage of microwave may result in RF leakage

Table of power densities from common RF sources

- "Power density," in units of microwatts per square centimeter ($\mu W/cm^2$), may be converted to watts per square meter (W/m^2)
- Table 1 describes the typical RF emissions from various RF sources[39]

Table 1. RF source, frequency, power, and power density

RF Sources	Frequencies	Power	Typical Average Power Density Exposure
Mobile Phone	GMS 850, 1900 MHz	0.3–3 W	1000 to 5000 $\mu W/cm^2$ (at ear)
Microwave Oven	2450 MHz	400–1200 W	5000 $\mu W/cm^2$ (at 5 cm)
WiFi	2.4 GHz and 5.0 GHz	less than 1.0 W (FCC) less than SC 6 (HC)	0.001–20 $\mu W/cm^2$ Max average RF exposure level 0.232% of SC 6 limits
TV Broadcast VHF	54–216 MHz	10–100 kW	0.005–1.0 $\mu W/cm^2$
TV Broadcast UHF	470–698 MHz	500–5000 kW	0.005–1.0 $\mu W/cm^2$
Smart Meter at 1 m	902–928 MHz	0.25 W	0.0001–0.002 $\mu W/cm^2$
FM AM	88–108 MHz 535 kHz–1.7 MHz	FM 33 kW AM 50 kW	0.005 to 1 $\mu W/cm^2$ 500 $\mu W/cm^2$

3.3 RF Sources Used in Industry

"CalStateArch_PreservationLab6"
courtesy of vlasta2, Flickr (CC BY-NC-ND)

- Frequencies: 135–6 MHz, 27.12 MHz, and 40.68 MHz[40,41]
- Heat sealer power: 1,500 W to 60,000 W
- Exposures: Unprotected worker exposures are often five to eight times above allowable exposure limits
- Body to ground currents: >200 mA

WorkSafeBC regulates permissible exposures to workers

Induction Heating (IH) Cooking Hotplates

- Frequency: 20–50 kHz, 26.1 kHz
- Power: commercial hobs: 1–3 kW
- Electric field strength: 10–20 V/m at 10 cm. Induced currents lower than HC SC6 guidelines[42]

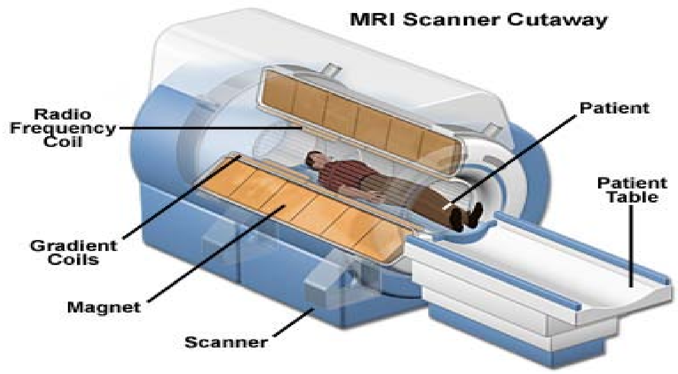
"Pressure Cooker on Induction Burner"
courtesy of Dinner Series, Flickr (CC BY)

3.4 EMF Sources Used in Medicine

Magnetic Resonance Imaging (MRI) in Radiology

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to visualize detailed internal structures. An MRI machine uses three different fields to generate images:

- A static magnetic field (average magnetic flux density of 1.5 to 3 Tesla) produced by a large magnet for the alignment of hydrogen nuclei (protons) inside the body.
- Low power time-varying magnetic field gradients (100 Hz to 1 kHz) generated by small magnets in three orthogonal directions to provide the spatial position of the protons. These MF gradients allow image slicing by focusing on the patient body part under examination.
- RF fields (10 to 400 MHz) to excite the protons (in the body) and cause them to emit radio waves for the acquisition of anatomical images.



"MRI Scanner" courtesy of onlinedocturs, Flickr (CC BY)

RF Ablation in Interventional Cardiology

Cardiac ablation is a procedure that can correct heart rhythm problems (arrhythmias).

It works by scarring or destroying tissue in the heart that triggers abnormal heart rhythms.[43,44]

- Frequency: 485 kHz, 915 MHz
- Power: 40 W, 50 W, 150 W

Physiotherapy: Short- Wave Diathermy

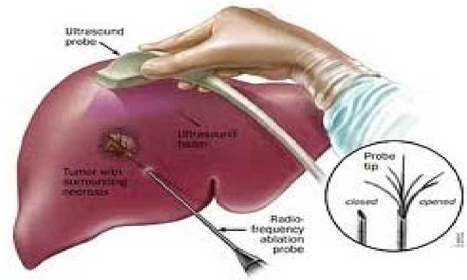
- Frequency: 27.12 MHz
- Power: 500 W

In diathermy, the heat generated by RF waves increases blood flow and speeds up metabolism and the rate of ion diffusion across cellular membranes. The fibrous tissues in tendons, joint capsules, and scars are more easily stretched when subjected to heat, thus facilitating the relief of stiffness of joints and promoting relaxation of the muscles and decrease of muscle spasms.[45]

"DA-ST-84-02519" courtesy of expertinfantry, Flickr (CC BY)

RF Tumour Therapy

- Frequency: 461 KHz
- Nominal power: 200 W
    - o Radiofrequency ablation – treats tumours in lung, liver, kidney and bone
    - o Needle-like RF ablation probe placed inside tumour
    - o RF waves increase temperature and destroy tumour
    - o May be combined with chemotherapy treatment[46,47]



"Radiofrequency ablation (RFA) in liver cancer (hepatocellular carcinoma)" courtesy of Hopkins Medicine.org (CC BY-NC)

Table 2. RF sources: frequency, power, and power density[48-55]

RF Medical Source	Frequencies	Power/Strength
Magnetic Resonance Imaging (MRI)	0 Hz	Main Magnetic Field operating field 1–7 Tesla
	100 Hz to 1 kHz	Gradient Magnetic Field 1–5 mT (millitesla)
	Radiofrequency fields 10–400 MHz	Up to a few KW Not radiative
Cardiac Ablation	485 kHz, 915 MHz	40, 50, 150, 200 W
Shortwave Diathermy	27 MHz	500 W
Tumour Therapy	461 kHz	200 W

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Section 4

Detection and Measurement of Radiofrequency Waves

Table of Contents

4.1 RF Exposure Metrics

4.1.1 RF field parameters

RF electromagnetic fields (EMF) are described by the following four parameters:

1. The frequency **F** (Hz) of the waves or the wavelength **λ** (m) which are related by:
2. $\lambda = \frac{c}{f}$ (c is the velocity of light) ***(4.1)***
3. The electric field intensity **E** in Volts per meter (V/m) at any point in space
4. The magnetic field strength **H** in Ampere per meter (A/m) at any point in space
5. The power density **S** in Watts per meter-squared (W/m^2) in the far field only where plane wave conditions apply

The magnetic flux density **B** in **SI** units of Tesla (T) or **CGS** units of Gauss (G) is also described as exposure from static magnetic fields.

4.1.2 Measurements in the near field region

The near field is the EMF from the RF source itself to a distance of one wavelength from the source.

In the near field region, the antenna gain and the angular distribution of the RF field vary with distance because of interactions between RF waves of different amplitudes and phases emitted from different segments of the RF antenna.

As a result, the relationship between the electric field **E**, the magnetic field **H**, and the power density **S** is unpredictable. Further, the measurements of the electric field intensity **E** and the magnetic field strength **H** at any point within the near field must be carried out independently.

Power density (RF power per unit area) measurements are inappropriate in the near field because of the non-uniformity of the RF field within a unit area.

4.1.3 Measurements in the far field region

The far field is the EMF located beyond the near field. In the far field, the antenna gain and the angular distribution of the RF field do not vary with distance. Hence, the relationships between the power density **S**, the electric field **E** and the magnetic field **H** in the far field are well defined, as shown below[1]:

$$S\left(\frac{W}{m^2}\right) = E\left(\frac{V}{m}\right).H\left(\frac{A}{m}\right) \quad \textbf{\textit{(4.2)}}$$

And:

$$E\left(\frac{V}{m}\right) = Z_0\ (\Omega)\,.\,H\left(\frac{A}{m}\right) \quad \textbf{\textit{(4.3)}}$$

Where **Z_0** is the impedance of free space. Since **Z_0** is equal to **377 Ω** in the far field, the relationships between **E**, **H** and **S** become:

$$E = 377\,.\,H \qquad \textbf{\textit{(4.4)}}$$

$$S = \frac{E^2}{377} \qquad \textbf{\textit{(4.5)}}$$

$$S = 377\,.\,H^2 \qquad \textbf{\textit{(4.6)}}$$

Therefore, it is sufficient to measure only one of the quantities **E, H** or **S** in the far field and to calculate the other two using equations ***(4.4), (4.5)****, or* ***(4.6).***

<u>Example</u>:

A surveyor is requested to carry out compliance power density measurements in a residential area located near GSM-900 base stations.

The maximum RF power density allowed for the public in Canada is $S_{limit} = \frac{6\text{ Watt}}{m^2}$ at a frequency of 900 MHz.

Suppose no power density probe is available and the surveyor needs to find an alternative. Since the measurements take place in the far field, the surveyor could use either an electric field probe to measure the electric field strength **E** or a magnetic field meter probe to measure the magnetic field strength **H** and compare the readings to the corresponding **E** or **H** limits.

The electric field limit E_{lim} and magnetic field limit H_{lim} corresponding to a power density of $\frac{6\text{ Watt}}{m^2}$ are:

$$E_{limit} = \sqrt{377\,S} = \sqrt{377 \text{ x } 6} = 47.56\text{ Volt/meter} \qquad \textbf{\textit{(4.7)}}$$

$$H_{limit} = \sqrt{\frac{S}{377}} = \sqrt{\frac{6}{377}} = 0.126\text{ Ampere/meter} \qquad \textbf{\textit{(4.8)}}$$

4.2 RF Detection Techniques

The detection and measurement of radiated RF waves is achieved by means of a measuring system consisting of an antenna (probe) and a receiver (Figure 4.1). For low RF levels, the signal passed on by the probe to the receiver needs to be amplified.

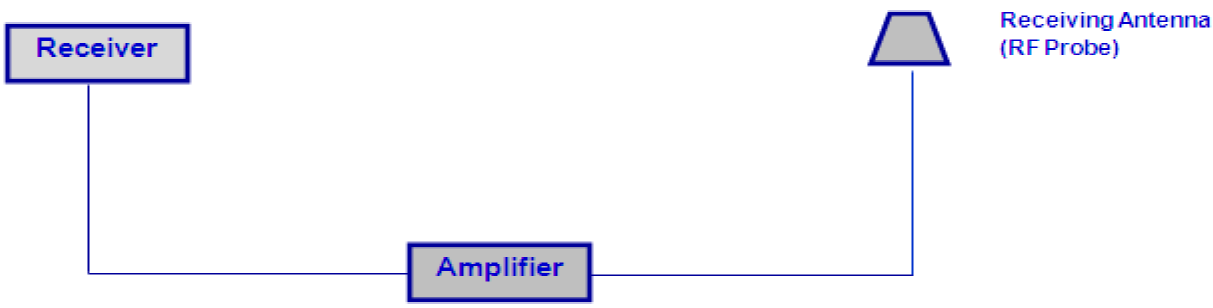

Figure 4.1 Schematic representation of a basic RF-measuring meter

4.2.1 RF detectors

Receiving RF antennas, also called RF probes, are devices designed to detect electromagnetic waves traveling through space. Some antennas serve both as receiver and transmitter of electromagnetic waves.

Probes come in different designs, depending on the purpose of use. Some are designed to be "broadband" antennas capable to receive or transmit RF waves over a large frequency range, while others are "narrowband" antennas designed to receive or transmit at some specific frequencies.

All receiving antennas are designed to capture electromagnetic energy and deliver the related signals to a receiver.

4.2.2 RF receivers

A receiver (or reader) is a device that collects the signal delivered by the antenna and processes it to extract needed information such as RF frequencies, electric fields, magnetic fields, power densities, etc.

4.2.3 RF survey meters

Portable RF-measuring instruments are adequate and practical for the detection of RF waves and the measurement of their strength (**E**, **H**, **S**).

For occupational exposure, the RF levels are usually measured close to the emitting antenna, while for public areas measurements are typically taken far from the source.

A standard RF survey meter is basically a combination of a receiving antenna (probe) and a meter.

Figure 4.2 Portable RF survey meter

4.2.4 Characteristics of RF survey meters

RF survey meters come in a variety of types and the choice of a particular meter is dictated by the type of RF environment to be surveyed: single source or complex RF fields, continuous or pulsed waves, near field or far field.

Industry Canada's "Guidelines for the Measurement of Radio Frequency Fields at Frequencies from 3 kHz to 300 GHz"[2] recommend a set of technical requirements to be considered in choosing a survey meter.

Table 4.1 lists the technical parameters of importance that should be provided for each survey meter.

Table 4.1 RF survey meter technical parameters

Parameter	Characteristics
Frequency range	Narrow band for known fields or broadband for unknown fields
Measurement range	Minimum and maximum RF exposure levels (**E** field, **H** field, power density **S**)
Linearity of the response	Percentage error over a range of exposure levels
Frequency sensitivity	Percentage error on the response over a frequency range
Directional response	• Isotropic probe: responds to incident signals in 3 directions X, Y, and Z. • Non-isotropic probe: responds to incident signals in only one or two directions in space
Continuous wave overload	Highest measurable exposure from continuous RF beams
Peak overload	Highest measurable exposure from pulsed RF beams
Calibration	Periodicity (usually every 2 years)
Environmental conditions	Influence of temperature and humidity on the response of the RF survey meter

4.2.5 Time- averaging of E, H, and S

Time-averaging is warranted when the exposure intensity changes with time. Therefore, time-averaged values of the electric field intensity **E**, the magnetic field strength **H,** and the power density **S** can be calculated on the basis of their respective sampled values.

For frequencies ranging from 100 kHz to 15,000 MHz, Health Canada Safety Code 6[3] specifies a time-averaging period of six minutes.

The time-averaged root-mean-square (rms) electric field E_{rms}, rms magnetic field H_{rms}, and rms power density S_{rms} can be obtained using the following formulas:

$$E_{rms} = [\frac{1}{6}\sum_1^n E_i^2 \ \Delta t_i]^{0.5} \quad (4.9)$$

$$H_{rms} = [\frac{1}{6}\sum_1^n H_i^2 \ \Delta t_i]^{0.5} \quad (4.10)$$

$$S_{rms} = \frac{1}{6}\sum_1^n S_i \ \Delta t_i \quad (4.11)$$

Where:

- E_i, H_i, and S_i are the sampled rms electric field, magnetic field, and power density readings, respectively, which are considered to remain constant in the i-th time period.

- Δti the interval time, in minutes, of the ith time period
- n the number of time intervals within six minutes

In addition, the sum of all time intervals Δt_i must be equal to six minutes:

$$\sum_{i=1}^{n} \Delta t_i = 6 \text{ min} \quad \textbf{(4.12)}$$

4.2.6 Spatial- averaging of E, H, and S

To determine the spatially averaged value of **E**, **H**, or **S**, local values (including the maximum value) are measured over the projected surface area (flat plane), equivalent to the head and trunk region of persons (adults or children) who would occupy the area of the incident fields. E_{rms},H_{rms} and S_{rms} can be calculated[3] as follows:

$$E_{rms} = [\frac{1}{n}\sum_{1}^{n} E_i^2]^{0.5} \quad \textbf{(4.13)}$$

$$H_{rms} = [\frac{1}{n}\sum_{1}^{n} H_i^2]^{0.5} \quad \textbf{(4.14)}$$

$$S_{rms} = \frac{1}{n}\sum_{1}^{n} S_i \quad \textbf{(4.15)}$$

- Where n is the number of locations and E_i, H_i, and S_i the electric field, the magnetic and the power density readings, respectively, are measured at the ith location.

4.2.7 Output of pulsed systems

The output of a pulsed system is expressed in terms of peak power P_{peak} and the average power P_{avg} is equal to the product of peak power by the duty cycle D_c:

$$P_{avg} = D_c . P_{peak} \quad \textbf{(4.16)}$$

4.3 Individual RF Monitors

Individual RF monitors (dosimeters), also called individual exposimeters, are direct-reading electronic devices worn by workers for the monitoring of their instant exposure to RF fields while carrying out their duties near RF sources.

Workers who are exposed over the long term to RF fields should wear individual RF dosimeters whenever they enter RF controlled areas to ensure that the exposure levels they are subjected to are below the occupational Limits of Health Canada Safety Code 6.

The exposure of individuals to RF fields is influenced by the following factors[4]:

- Location of the exposed person with respect to the surrounding RF sources
- Traffic, fading, and power variation of RF signal
- Frequency of the RF waves
- Polarization and direction of arrival of incident electromagnetic fields

The first RF personal dosimeter was designed to measure RF exposure from mobile phone base stations.[5]

A practical personal RF dosimeter should have the following properties:

- Small, light in weight, and reasonable in cost
- Direct-reading (display)
- Broadband response to cover the entire RF spectrum
- Isotropic (reading independent of direction)
- Near field and far field readings
- Large measurement range of electric field and power density
- Capable of data recording

4.4 Absorption of RF Waves – SAR

The absorption of RF waves in the human body is important in the frequency range 100 kHz–10 GHz and is expressed by the Specific Absorption Rate (SAR). SAR is the rate of RF energy absorbed per unit mass of tissue. It is defined in units of Joules per second per kilogram (J/s/Kg) equivalent to Watts per kilogram (W/kg).

According to the International Commission on Non-Ionizing Radiation (ICNIRP), SAR is important in the frequency range 100 kHz–10 GHz and must be determined for situations where exposure of the whole body or parts of the body takes place at a distance of 20 cm or less from the RF source.[2,3] However, SAR cannot be measured directly in human tissue. Instead, it can be estimated by the three methods described below.

4.4.1 Determination of SAR by a calorimetric method

The calorimetric method[2] uses a temperature probe inserted in a tissue-like phantom to measure the rate of temperature increase $\frac{\Delta T}{\Delta t}$ in the phantom generated by absorption of RF waves.

“Human phantom SAR” courtesy of Indexsar.com (CC BY-NC-ND)

Figure 4.3 Example of a head phantom for SAR measurements[6]

SAR is determined by calculating the heat produced within a unit mass of the phantom as follows:

$$\mathrm{SAR}\left(\frac{\mathrm{W}}{\mathrm{Kg}}\right) = \mathrm{C}\left(\frac{\mathrm{J}}{\mathrm{Kg}\ {}^{\mathrm{o}}\mathrm{C}}\right) . \frac{\Delta \mathrm{T}({}^{\mathrm{o}}\mathrm{C})}{\Delta \mathrm{t}(\mathrm{sec})} \qquad \textit{(4.17)}$$

- Where C is the specific heat capacity of the phantom material, in J/(kg ºC)

In Equation (4.17), the rate of temperature increase is assumed to be linear during the test with no thermal losses.

4.4.2 Assessment of SAR by E- field measurements

The E-field method measures the root-mean-square electric field $\mathrm{E_{rms}}$ induced inside a tissue-simulating phantom (e.g., Figure 4.4) by an external RF field by means of implantable electric field probes.

“Human phantom SAR” courtesy of Indexsar.com (CC BY-NC-ND)

Figure 4.4 Example of a head phantom assembly for inner probe measurements[6]

SAR is then determined using the formula[3]:

$$\mathrm{SAR} = \left(\frac{\sigma}{\varrho}\right) \mathrm{E_{rms}^2} \qquad \textit{(4.18)}$$

Where:

- σ is the electrical conductivity of body tissue in units of Siemens per meter (S/m)
- ϱ, the mass density of tissue in Kg/m[3]
- $\mathrm{E_{rms}^2}$, the rms electric field squared in V^2/m^2 induced in the tissue-like phantom

The dielectric properties of tissue play an important role in the absorption of RF waves by the body. Table 4.2 gives values of the relative dielectric constant (**ε**), the electric conductivity (**σ**), and the penetration depth (**δ**) for muscle tissue at various RF frequencies.[7]

Table 4.2 Approximate dielectric parameters for muscle tissue at various frequencies

Frequency	Relative Dielectric Constant (ε)	Conductivity (σ), in Siemens/Meter	Penetration Depth (δ), in Centimeters
100 kHz	1850	0.56	213.0
1.0 MHz	411	0.59	70.0
10 MHz	131	0.68	13.2
100 MHz	79	0.81	7.70
1 GHz	60	1.33	3.40
10 GHz	42	13.3	0.27
100 GHz	8	60.0	0.03

Important: If the RF field is not continuous but pulsed, the pulse duration and the pulse repetition rate are necessary for the determination of the duty cycle of the RF generator.

4.4.3 Determination of SAR by a graphical method

SAR values can be determined from a graph as shown in Figure 4.5.[8]

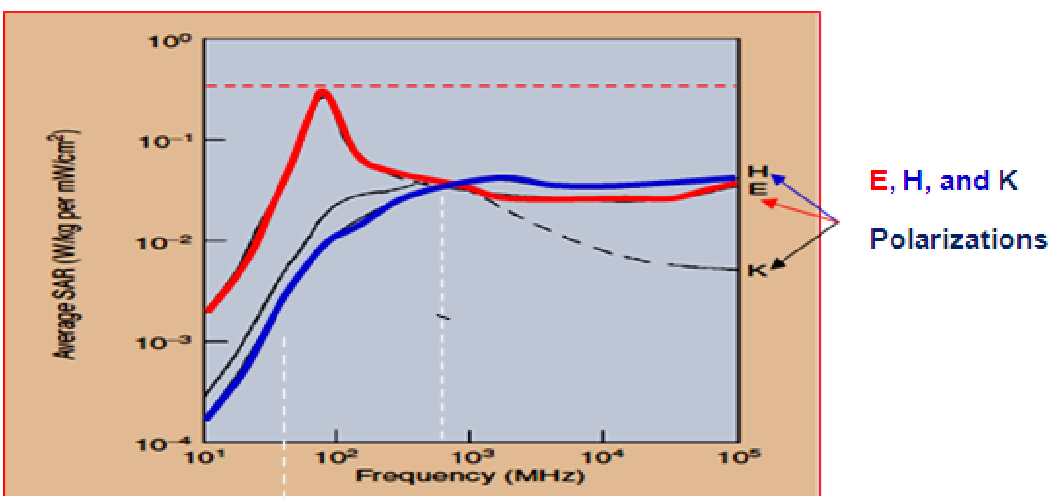

Figure 4.5 Calculated whole-body average SAR (W/Kg per mW/cm²) versus frequency for models of the average man for three standard polarizations

On the Graph:

- E-polarization is where the electric field **E** is parallel to the main axis of the body
- H-polarization is where the magnetic field **H** is parallel to the main axis of the body
- K-polarization is where the direction of propagation of RF waves is parallel to the main axis of the body
- The highest RF absorption occurs for **E**-polarization at frequencies 70 to 80 MHz.
- At about 700 MHz, the SAR is the same for all three polarizations.

For conditions where SAR determination is not practically possible, the measurement of field strength (**E** or **H**, near field, far field)) or power density (far field only) can be carried out as an alternative.

4.4.4 SAR measurements in time- varying RF fields

Note: If the RF exposure changes with time, the time-averaged SAR over a period of six minutes can be calculated as follows[3]:

$$\mathrm{SAR} = \frac{1}{6}\sum_{i=1}^{n}(\mathrm{SAR})_i\,\Delta t_i \qquad (4.19)$$

Where:

- $(\mathrm{SAR})_i$ the sampled SAR in the i-th time period
- Δt_i the time interval of the i-th time period

4.5 References

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Section 5

Assessment of Radiofrequency Exposure to the General Public

Table of Contents

Summary

- Use of radiofrequency field (RF) emitting devices near the body (in the near-field) increases personal exposures. The highest typical personal exposure to RF is from the use of a mobile phone at the head. The most important contributor to the intensity of this exposure is the type of technology (e.g., Global System for Mobile Communications (GSM) output power levels are several times higher than Code Division Multiple Access (CDMA) levels in the field).

- Additional engineering factors that affect output power levels of mobile phones and other RF emitting devices include adaptive or power control, duty cycle, frequency, and size of antenna.

- Environmental factors that affect the intensity of exposure of mobile phones include location (indoors vs. outdoors, urban vs. rural, presence of buildings/obstacles) and being in transit, particularly in buses and trains.

- Once in the far field of local RF-emitting devices, the exposure levels decrease substantially with increasing distance (inverse square law), but levels are affected by reflections from buildings and other obstacles.

- Ambient exposures, which are natural and man-made environmental exposures the general public may receive even when not directly using RF devices, are several orders of magnitude (up to millions of times) lower than exposures received when using a mobile phone at the head. Exposure from mobile phones and DECT cordless phones (even when not in use), FM broadcasting, and microwave ovens can be important contributors to background exposure to RF.

- Although most studies indicate that personal exposures to RF from individual sources are low (below exposure limits), the increasing number of sources in combination with increasing duration of use may potentially increase total exposures over time, offset to some extent by improvements in technology. Continued assessment of new and emerging technologies, as well as of overall personal exposures to RF sources, will be useful in determining trends over time.

5.1 Introduction

In addition to low levels of exposure to natural sources of RF, principally from sunlight, exposure to electric and magnetic fields from man-made sources of RF such as radio and television transmitters and mobile communications is almost universal. Accurate assessment of exposure is critical in determining exposure-response relationships in epidemiological studies on the health effects of RF. Surrogates of exposure to RF from mobile phone use obtained by surveys are most commonly simple estimates of hours/minutes or number of calls over a specific period of time. These indices are usually obtained by questionnaire or interviews in observational studies. In addition to

assessment of time by duration and frequency of occurrence, assessment of intensity (output power in the case of RF) is an important exposure index.

In assessing intensity of exposure, an understanding of possible biological mechanisms informs the exposure assessment strategy. Biological models for how exposure might affect disease outcomes include cumulative, threshold, repetition, and rate of change models. Most epidemiological studies derive exposure assuming a cumulative exposure model (using total duration of calls as a measure of exposure) or a repetition model (number of events of RF exposure). But a criticism of using cumulative or repetition models is that they do not differentiate between low intensity and high intensity exposures. For example, using a cumulative model would not be appropriate when assessing temperature and duration of immersing a hand in water, as health effects would be expected at 100°C for one minute but not at 20°C for five minutes, even though the cumulative exposure would be the same.

Also affecting intensity of exposure is the fact that RF can be reflected, absorbed and transmitted. RF at frequencies used in telecommunications penetrates into the body tissues for a few centimetres. Energy is not deposited uniformly throughout the body and RF becomes less penetrating into body tissues as the frequency increases.[1]

The objective of this section is to compare exposure measurements for various RF emitting devices, describe what factors affect exposure, and determine the typical daily exposures to RF experienced by the general population.

The type of data collected in exposure studies include output power of sources usually in units of watts (W) or decibels in the logarithmic scale referenced to 1 mW (dBm) and electric field strength in units of Volts per meter (V/m) or power density (W/m^2), at specified distances in the far field. Absorption into body tissues is proportional to output power (W), power density is proportional to output power, and electric field strength is proportional to the square root of output power.[2] However, for near field exposures from devices held close to the body like mobile phones or tablet PCs, power density and electric field strength measures do not apply and instead, Specific Absorption Rate (SAR) is calculated in W/kg as a dosimetric measure.

When reviewing the exposure data from these studies, reference can be made to the exposure limits for total exposures and for various RF frequencies (see Section 13).

5.2 Methods

The literature search strategy for the "exposure assessment" of RFs was carried out using the EBSCO, OvidSP, and Embase databases. EBSCO databases were searched first in stages, with each search expanding upon the previous key terms and phrases. The results were then compared to determine whether or not the additional terms aided in the precision of the results. It was found that phrases such as "exposure assessment" and strings of words such as (radiofrequency OR radio-frequency OR "RF" OR

electromagnetic fields) proved effective in retrieving relevant results. Once the search terminology was established and a large collection of relevant sources was collected in EBSCO, the searches were essentially replicated in OvidSP and Embase, although little additional material was uncovered. As a final check, World Cat was searched using the broad term "electromagnetic frequency" to scan for additional articles, and a small selection of articles were added.

Suggested search terms:

Exposure assessment	Radiofrequency	RF-emitting devices
"exposure assessment"	radiofrequency OR radio-frequency OR RF OR electromagnetic fields	cell* phone* OR cellular mobile phone* OR wi-fi OR wifi, wireless OR wireless internet OR microwave* OR "smart meter"OR "base stations"

Sixty-four abstracts were originally reviewed. Criteria for inclusion were papers which included measurements of RF sources and/or mention of factors that affected exposure in terms of output power, power density or SAR. Of those 64 abstracts, 22 were deemed relevant and retrieved articles were reviewed in their entirety. Papers were back referenced to identify an additional 15 articles. For the most part, only recent literature published after 2005 was considered.

To enable comparison, we attempted to use the same units to describe output power in Watts (W), power density (mW/cm^2), and SAR (W/kg averaged over 10g[1]). We converted electric field strengths V/m to mW/cm^2 using an RF calculator.[6] We also converted all power density measurements to mW/cm^2 to enable comparisons. For example, 1 mW/m^2 was divided by 10,000 to convert to 0.0001 mW/cm^2. The values in mW/cm^2 can then be compared to Health Canada Safety Code 6 limits (e.g., for microwave frequencies of 2.4 GHz, the limit is 1 mW/cm^2). Where conversions were not possible, we have noted the original units in the table of results (Tables 1 and 2).

[1] In Europe, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) SAR guideline[3] is 2 W/kg averaged over 10 g for localized head and trunk, whereas the Federal Communications Commission (FCC) and Health Canada uses 1.6 W/kg averaged over 1 g for head and trunk.[4,5] As all studies were conducted outside of North America, SAR was often reported as averaged over 10 g.

5.3 Results

The exposure studies were categorized into three major types:

1) **Source measurements in the field.** These studies used either spectrum analyzers or phantom models brought into the field. In the case of mobile phones, occasionally, dose phones (software modified phones) were sometimes used to collect power control levels that serve as surrogates for actual output power levels.

2) **Source measurements in the laboratory.** SAR measurements were ascertained in the laboratory using either real devices or antennas emitting at frequencies that were relevant to RF emitting devices.

3) **Personal exposure or area measurements.** For personal exposure assessment, total RF measurements were obtained by using dosimeters and daily logs to determine probable sources. For area measurements, a spectrum analyzer was placed in different locations to determine ambient exposure.

Table 1 provides measurements from recent studies of output power levels or power densities of RF for specific sources. The RF devices include wireless phones and phone technologies, wireless local area networks, Smart Meters, mobile phone base stations and other sources (e.g., microwave ovens, radio/TV broadcasting). The units for output power are consistently given as mW. Power density units are mW/cm^2 unless specified as V/m. Note for all the tables that because the methods of exposure assessment vary somewhat between studies, the values can be compared for different exposure devices within a study, but not between studies.

Table 1. RF output power and power density levels for specific sources of RF*

RF Source	Frequency	Location; Distance	RF Power Output (mW)	RF Power Density (mW/cm^2)	Reference
WIRELESS PHONES					
Mobile phone	900 MHz, 1800 MHz	California; At ear during call		1-5	Electric Power Research Institute (EPRI) (2011)[7]
Analog	850 MHz	California; At ear of phantom	171.4 (overall average)		Kelsh et al. (2011)[8]
TDMA	850 MHz	California; At ear of phantom	66.53 (overall average)		Kelsh et al. (2011)[8]
GSM	1900 MHz	California; At ear of phantom	25.76 (overall average)		Kelsh et al. (2011)[8]

RF Source	Frequency	Location; Distance	RF Power Output (mW)	RF Power Density (mW/cm^2)	Reference
GSM software modified phones	1900 MHz	California; At ear of phantom Rural Suburban Urban	43 (average) 35 (average) 25 (average)		Kelsh et al. (2011)[8]
GSM (ambient, not during use)	900 MHz	Urban (Basel) Rural (Bubendorf)		0.16 V/m (avg, urban) 0.10 V/m (avg, rural)	Burgi et al. (2008)[9]
GSM (ambient, not during use)	1800 MHz	Urban (Basel) Rural (Bubendorf)		0.42V/m (avg, urban) 0.04 V/m (avg, rural)	Burgi et al. (2008)[9]
UMTS (ambient, not during use)		Rural (Bubendorf)		0.02 V/m (avg., rural)	Burgi et al. (2008)[9]
WCDMA (used in UMTS networks in Europe)		Europe; At ear	Big City – 0.2 Small City – 0.4 Buildings – city 1.1 Market Centers – 5 City Driving – 0.15 Highway – 0.3 Outdoor – < 1 Indoor – < 5		Gati et al. (2009)[10]
DECT phones	1.9 GHz	At base station or handset: 1 vs. 6 calls	Station: 10; 60 At Handset: 10; 10 Idle Station: 2.5		Swiss Federal Office of Public Health (FOPH) (2011)[11]
WIRELESS LOCAL AREA NETWORK					
WLAN	2.4-5 GHz	California; 3 feet		0.0002-0.001 0.000005-0.0002	EPRI (2012)[7]
WiFi (laptop)	2.4 GHz	US, France, Germany, Sweden; 1 m		0.004 (maximum time-averaged – integrated power density 70-3000 MHz)	Foster (2007)[12]
WiFi laptops and access points	2.4 GHz	UK; 0.5 to 1.9 m in 10 cm steps	Spherically integrated radiation power (IRP): laptops – 5-17 access points – 3 to 28	Laptops: 0.0022-0.000013- (max) Access points: 0.0087- 0.00022-	Peyman et al. (2011)[2]
WiFi laptops and access points	5 GHz	UK; 0.5 to 1.9 m in 10 cm steps	Spherically integrated radiation power (IRP): laptops – 1 to 16 access points – 3 to 29		Peyman et al. (2011)[2]

RF Source	Frequency	Location; Distance	RF Power Output (mW)	RF Power Density (mW/cm²)	Reference
WiFi laptops and access points	2.4 GHz	UK; 1 m	Laptops: 17-57 Access points: 16-229	Laptops: 0.0002-0.0005 Access points: 0.0001-0.0018	Peyman et al. (2011)[2]
WiFi laptops and access points	5 GHz	UK; 1.5 m	Laptops: 5-45 Access points: 17-165	Laptops: 0.00002-0.0002 Access points: 0.0001-0.0006	Peyman et al. (2011)[2]
SMART METERS					
Smart Meters	900 MHz, 2400 MHz	California; 3 feet		0.0001 (250 mW, 1% duty cycle) 0.002 (1 W, 5% duty cycle)	EPRI (2011)[7]
Smart Meters	900 MHz, 2400 MHz	California; 10 feet		0.000009 (250 MW, 1% duty cycle) 0.002 (1 W, 5% duty cycle)	EPRI (2011)[7]
Smart Meters	900 MHz (RF LAN) 2400 MHz (HAN Transmitter) Cell relay 850 MHz Cell relay 1900 MHz	California; Power output at surface (not taking into account duty cycle)	126 (0.5th %ile) 257 (50th %ile) 398 (99.5 %ile) 39.8 (0.5th %ile) to 114.6 (99.5 %ile) 1514 (max, GSM) 326 (max, CDMA) 741 (max, GSM) 305 (max, CDMA)		Tell et al. (2012)[13]
Smart Meters	900 MHz	BC; 30 cm 1 m 3 m (0.07% duty cycle)		0.0032 0.002.02 0.001.17 (one active Smart Meter)	British Columbia Centre for Disease Control (2012)[14]
MOBILE PHONE BASE STATIONS					
Mobile base stations		Germany; Different distances		3x10E-10- 0.07152	Bornkessel (2011)[15]
Mobile phone base station	900 MHz, 1800 MHz	Germany; 10s to a few thousand feet		0.000005-0.002	EPRI (2011)[7]
GSM Mobile phone base station (simulated)	900 MHz	Germany; 49-704 m		3.4x10E-09-0.000783	Bornkessel et al. (2007)[16]
UMTS base station (simulated)	2100 MHz	Germany; 49-704 m		1x10E-08- 0.00693	Bornkessel et al. (2007)[16]

RF Source	Frequency	Location; Distance	RF Power Output (mW)	RF Power Density (mW/cm²)	Reference
GSM WCDMA WiMAX Base stations	Wideband spectrum 75 MHz– 3 GHz	Saudi Arabia 10 m to peak distance of 39–501 m	60 base stations worst case: 21.96 (wideband)	Most values: GSM900: 1 x10E-8 to 1 x 10E-7: GSM1800 & UMTS: 1 x 10E-9 to 1 x10E-8	Alhekail et al. (2012)[17]
OTHER SOURCES					
Microwave ovens	2450 MHz	California; 2 inches; 2 feet		5 0.05–0.2	EPRI (2011)[7]
Microwave ovens	2450 MHz	<5 cm		New: 0.08 (avg) Old: 50% <0.062, 0.17, 0.41 (avg)	Alhekail (2001)[18]; Matthes (1992)[19]; Than-sandote (2000)[20]
Radio/TV broadcast station	Wide spectrum	Far from source (in most cases)		0.001 (highest 1% of population) 0.000005 (50% of population)	EPRI (2011)[7]
FM radio		Urban (Basel) Rural (Bubendorf)		0.03 V/m (avg, urban) 0.02 V/m (avg, rural)	Burgi et al. (2008)[9]
Digital Audio Broadcasting		Urban (Basel) Rural (Bubendorf)		0.00 V/m (avg, urban) 0.00 V/m (avg, rural)	Burgi et al. (2008)[9]
TV		Urban (Basel) Rural (Bubendorf)		0.03 V/m (avg, urban) 0.04 V/m (avg, rural)	Burgi et al. (2008)[9]

5.3.1 Mobile phones

The bulk of the scientific literature on RF exposure assessment has been on mobile phones. The currents and charges on the metal parts of the mobile phone form the reactive near-field (5 cm for 900 MHz, 2.5 cm for 1900 MHz).[21] Cellular networks are designed to operate so that the voice quality of one channel (one frequency) is limited by the interference of other signals using the same frequency in other parts of the cellular systems.[21] For current mobile phones, the network uses power control or adaptive control, which reduces RF power to a minimum level compatible with voice quality for a conversation.[21]

Many factors can change the intensity of exposure including technology, location, transit, and usage of the phone.

5.3.1.1 Technology

The type of technology appears to be the most important variable in explaining differences in intensity of exposure of mobile phones. In the early 1980s, first generation (1G) analog phones were introduced using a FDMA (frequency division multiplexing access) where frequency was modulated to communicate between the mobile phone and base station. Second generation (2G) phones were introduced in the 1990s with TDMA (time division multiple access) or CDMA (code division multiple access) technology. In TDMA technology, the channel can be shared by establishing time slots assigned to each user. Global System for Mobile Communications (GSM, based on TDMA technology) uses eight slots. The assignment of one slot per user gives rise to the pulsed nature of the wave; for example, a GSM phone will only be transmitting for 1/8th of the transmission time (1/8th duty cycle).[11] CDMA uses a different code to allow for multiple users to use the same channel, and therefore the transmission is continuous.

Third generation phones (3G) include Universal Mobile Telecommunications System (UMTS) wide-band CDMA (WCDMA) and High Speed Downlink Packet Access (HSDPA). Many of the phones in use today are considered 3.5 G, meaning the phones have additional data streaming features but use a 3G network (e.g., smartphones).[22] Some networks have started converting over to 4th generation (4G) networks which will allow 4G phones to be better able to stream more data faster, providing a mobile broadband version of a laptop computer. The 4G technologies include Long Term Evolution (LTE), and WiMAX (Worldwide Interoperability for Microwave Access), which are based on FDMA-type technologies

The output power of mobile phones is described as peak output power, maximum output power, or actual output power. Peak output power is the phone's maximum possible power level, whereas maximum output power is the phone's maximum power level within a network. For instance, the peak output power of GSM can be 1W or 2W, but because GSM only transmits for ⅛th of the call time and every 26th pulse is omitted, the maximum output power is 120 mW or 240 mW.[11] For CDMA and UMTS technologies, the transmission is continuous, and therefore the peak and maximum output power are the same at 250 mW.

Actual output power is usually lower than maximum output power due to adaptive or power control (which reduces RF power of mobile phones to a minimum level compatible with voice quality for a conversation).[21] Some studies report that adaptive control for GSM phones can decrease RF output by 50% of the maximum output power levels.[23,24] In the German Mobile Telecommunication Programme study, GSM operation produced average output power levels between 10 and 70% of maximum output power and maximum output power was only reached during 5 to 30% of the call time.[15] Discontinuous transmission (DTX) in GSM technology, which allows for transmission only during speaking, can also decrease output power levels by 30%.[23,24] Similarly, with

CDMA or WCDMA technology, when the user is not speaking, the mobile phone runs at ½ or ⅛ of maximum output power.[25]

Mobile phones using different technologies and frequency bands have different peak output power. For instance, in a study of 1G and 2G phones, the phones that were used had a range of nominal peak output power levels ranging from 250 mW to 2 W, but in real-world scenarios, the average power levels were much lower (Table 1, Figure 1).[8] In this study, analog technology produced the highest average power levels, followed by TDMA, GSM, and CDMA. CDMA produces RF up to hundreds of times lower than the other technologies.[8] The output power of UMTS 3G mobile phones was a hundred times lower than that of GSM phones in one study.[26]

The reason analogue phones (which are no longer in use) produced the highest RF output power levels is related to the fact that no power control was available and they were always operating at maximum power. The 2G and newer technologies all utilize power control. GSM has some unique features that make it different from the other technologies in that the phone transmits at peak power each time there is a handover of the signal from one base station to another ("hard" handover); as a result, the more handovers there are (such as might be experienced by driving or moving quickly), the higher total number of peaks and average power.[15] Due to this handover phenomenon for GSM phones, very short calls can produce higher average output power levels because the first connection to the base station occurs at maximum power before dropping to a lower power level.[27]

CDMA technology was originally developed by the US military to transmit near background levels of RF.[28] Therefore in real-world scenarios, it transmits the lowest level of power of the 1G and 2G technologies.[8] CDMA in Canadian systems has a power control of 800 times per second.[29] WCDMA (3G) technology used in UMTS networks in Europe uses even faster power control at a rate of 1500 Hz instead of GSM which varies at a rate of 16.6 Hz (once every 60 ms). This faster power control means that WCDMA and CDMA devices can connect with more than one base station at a time during a handover ("soft" handover) so they can avoid maximum power emissions when handover occurs.[10]

5.3.1.2 Hands-free kits

Hands free kits, such as wired headsets, are effective in reducing exposure to RF. For example, SAR at the head when using a headset was found to be 8–20 times lower than when making calls holding the phone to the ear.[30] Kuhn et al. confirmed the findings but notes the possibility of localized exposure enhancement due to EMF from the electrical part of the device in the ear.[31]

5.3.1.3 Location

Study location is an important predictor of exposure.[24,32] Studies have shown that output power levels of mobile phones used in rural areas are higher than in urban areas, likely due to lower base station densities in rural locations.[8,10] Presence of obstacles such as buildings impact RF.[9] Average emitted power is usually greater indoors compared to outdoors as building features interfere with signals.[10,33]

5.3.1.4 Transit

For GSM mobile phones, being in motion while in a car or other mode of transportation tends to increase average output power as handovers are characterized by maximum peaks.[8,34] CDMA phones utilize soft handovers and therefore movement does not influence the output power of CDMA as much (as long as base stations are available for handovers).[8] However, for UMTS phones, moving was observed to increase output power.[11,26] Some studies show that being in transit (particularly in trains or buses) produces the highest total ambient field exposures,[33] which is likely due to the GSM handover phenomenon, but may also be due to the high use of wireless devices on trains and buses.

5.3.1.5 Other factors

One study showed that for data transfer there is up to a four times increase in output power than for voice for wCDMA technology. However, while the output power increases during data transfer, distancing of the phone from the body (e.g.,10 cm away from the head) attenuates the exposure.[10] Other research on UMTS phones has shown that data upload can produce output power levels that are about 30 times higher than a stationary call (and about 14 times higher than a moving call). Also, mobile phones continue to transmit when on, but not in active use. GSM phones transmit once every 12–240 minutes and UMTS once every 5–720 minutes.[11]

Different models of phones using the same technology do not show substantial differences in output power, particularly in comparison to technology or urban/city differences.[8,24]

5.3.1.6 Specific Absorption Rates (SAR) of mobile phones

Dosimetry is used to evaluate the induced electric fields in the body from exposure to near-field RF sources through either experimental modelling or numerical calculation of SAR in Watts per kilogram. For frequencies higher than 100 kHz, such as RF from mobile phones, the SAR links the strength of exposure of an external RF field (power density) to the effect of a temperature rise inside the body due to vibration of molecules.[1] Before mobile phone models are permitted for sale, SAR testing is required by agencies like International Commission on Non-Ionizing Radiation Protection (ICNIRP) in Europe and Federal Communications Commission (FCC) in the US to ensure that phones do not expose the general public to levels above safety guidelines. SAR

measured for compliance consists of forcing phones to maximum output power and measuring the SAR in phantom heads (models of human heads with similar dielectric properties of the human head). When CDMA phones are forced to maximum output power, the SAR surpasses GSM and TDMA phones.[26] However, in the field CDMA transmits power on average hundreds of times lower than the nominal maximum output power level.[8] Therefore compliance testing evaluates the worst-case exposures from mobile phones, which can be substantially lower in real-world scenarios.

Some of the studies that were reviewed measured SAR by simulating maximum output power levels in specific frequency bands (representing RF devices but not using the actual devices in the studies) at the head or body. In these worst-case scenarios, SAR levels were often above current standards.[35,36] However, several studies have attempted to evaluate more realistic SAR using phantom heads and whole body models in the laboratory, and several factors have been shown to influence SAR. Distance of the RF source from the head is an important factor to consider. The absorbed power for a mobile phone placed 10 cm from the head decreases more than 10 times than when it is held close to the ear. At 40 cm from the head, the maximum SAR over 10g is close to 1% of the SAR obtained by touching the phone to the head [10]

Lower frequency RF tends to penetrate more deeply into brain tissue. A study by Kuhn et al. (2009) showed that average peak SAR of phones from the FCC database at 1900 MHz were lower than those at 850 MHz.[26] Another study by Togashi et al. (2008) showed that a fetus averaged SAR and fetal brain averaged SAR exposed to mobile radio terminal RF at 900 MHz were more than five times higher than those at 2 GHz.[38] However, there are two resonance frequency ranges where more absorption in tissue occurs: between 2100–2400 MHz there is greater RF absorption at the skin, whereas at a lower resonance frequency of ~100 MHz, RF is absorbed more in the muscle and fat, resulting in higher SAR values in these regions.[37]

Whole body exposure at frequencies in the range of 80 to 180 MHz and 1–4 GHz to ICNIRP reference exposure levels may expose children and small persons (shorter than 1.3 m) to above acceptable ICNIRP SAR levels.[15] A 2010 study by Christ et al. on GSM phones did not find differences for peak spatial SAR (defined as the maximum value of SAR averaged over 10 g) between an adult head model and children models (3, 6, and 11 year old).[39] However, local SAR (without spatial 10 g averaging) for children showed higher exposure of some tissues and organs such as sub-regions of the brain (cortex, hippocampus and hypothalamus) and in the eye due to closer distance to the phone, whereas other head regions were lower than adults. A large increase in induced fields for children's bone marrow was attributed to its higher conductivity compared with that of adults.[39]

In Table 2, representative SAR values are given for wireless phones, WLAN and other sources of RF. The assessment of SAR depends on the performance of the electric field probe, the phantom dimensions, the dielectric properties of the tissue used and the

exposure conditions. Typically, a 30% expanded uncertainty is reported for mobile phone SAR measurements.[1] Values found are not directly comparable between studies due to differences in methodology, including type of antenna used and characteristics of the phantom model.

Table 2. SAR values for specific source of RF

RF Source	Frequency	Distance	Description	SAR (10 g W/kg)	Reference
WIRELESS PHONES					
Smart phones & mobile phones	GSM 900, GSM 1800, UMTS		140 phones Left and right ear of head model	0.168–1.61 Median: 0.817	Bornkessel (2011)[15]
Simulated mobile phones systems	900 MHz at 1 W	40 mm & 10 mm	half-wave dipole antennas & planar inverted F antenna	Fetus 1.2–1.4, Fetal brain 1.8–2.9 Mother 0.8–1.1 (estimates from graph)	Togashi et al. (2009)[38]
Simulated mobile phones systems	2 GHz at 1 W	40 mm & 10 mm	half-wave dipole antennas & planar inverted F antenna	Fetus 0.1–0.25, Fetal brain 0.05–1.5 Mother 0.2–1.0 (estimates from graph)	Togashi et al. (2009)[38]
Simulated mobile phone	1850 MHz	125 mW, at head	10-year old child phantom and adult	Child: 0.596 (10g); 0.885 (1g) Adult: 0.362 (10 g 0.527 (1 g)	De Salles et al. (2006)[35]
Simulated mobile phone	850 MHz	600 mW, at head	10-year old child phantom and adult	Child: 2.05 (10 g); 2.89 (1 g) Adult: 1.7 (10 g); 1.8 (1 g)	De Salles et al. (2006)[35]
Cordless phones (DECT)	1880–1900 MHz		4 handsets	0.01 to 0.05	FOPH (2011)[11]
WIRELESS LOCAL AREA NETWORK					
WLAN	2, 4 GHz	Worst case	Using maximum output power and data rate; Using ISEE 802.11g	Access point: 0.27 PC card: 0.11	Kuhn cited in FOPH (2011)
WiFi (laptop)	2.4 GHz	34 cm	Using inverted F antenna operating at peak power of 100 mW, duty factor of 1, highest localized SAR at head	0.0057 head	Findlay et al. (2010)[36]

RF Source	Frequency	Distance	Description	SAR (10 g W/kg)	Reference
OTHER SOURCES					
Microwave ovens	2450 MHz	<0.1 cm 5 cm 30 cm	With microwave oven emitting at maximum permitted leakage level (5 mW/cm² at a distance of 5 cm)	< 0.1 cm: 7.95 5 cm: 0.256 30 cm: 0.0056	Bangay and Zombolas (2003)[40]
Baby monitors	446 MHz	Worse case	Devices at 500 mW peak power continuously	0.08	FOPH (2011)[11]
	863	Worst case	10 mW peak power continuously	0.01	FOPH (2011)[11]
Simulated Portable radio terminal	900 and 2000 MHz			0.007 and 0.0004 (peak fetus 10 g SAR, right arm, –60°)	Akimoto et al. (2010)[41]

*values estimated from bar chart (Figure 8)[38]

5.3.2 Cordless phones

Cordless phones are wireless handsets that communicate with a base station connected to a fixed telephone line. Multiple frequency bands exist, with the most common in North America being 900 MHz, 1900 MHz, 2.4 GHz, and 5.8 GHz. Digital Enhanced Cordless Telecommunications (DECT) phones, which utilize the 1900 MHz band, are most commonly used in Europe and are also used in North America. As most of the RF exposure literature originates in Europe, only data for DECT cordless phones are reported here.

DECT phones produce pulsed emissions. A 10 millisecond frame is divided into 24 time slots. When a call is in progress, a handset transmits during one of these slots and receives a signal from the base station during a timeslot 5 milliseconds later. The base station can communicate with up to six handsets at a time. When no calls are in progress, the base station transmits a brief pulse every 10 milliseconds. In certain models, the base station never transmits when the handset is placed in the cradle.[11] The peak output power for DECT phones is 250 mW, but because the transmission is pulsed, the average output power is lower, typically 2 mW. Cordless phones (DECT) do not usually implement power control like most modern mobile phones, although some energy-efficient models regulate power so that output power decreases when the connection is good.[11] For this reason, SAR from cordless DECT phones can be higher than SAR from UMTS phones (but can be up to five times lower than GSM phones).[42] In a study of six telephone calls, the power at the DECT base was 60 mW and at the handset was 10 mW. In the idle state, the power at the base was 2.5 mW and 0 mW at the handset (Table 1, Figure 1).[11] SAR measurements for four handsets ranged from 0.01 to 0.05 W/kg (Table 2).[11]

5.3.3 Mobile phone base stations

The mobile phone network is divided into "cells," each with its own macrocell base station typically mounted on a rooftop to send and receive radio signals. Output powers are typically of tens of watts and macrocells cover distances from 1 to 10 km. Microcells have output power of up to a few watts and cover several hundred meters. Picocells are used in dense areas such as airport terminals and shopping centers and have output powers of up to 100 mW. Public exposure from mobile phone base stations is much lower than that from mobile phone use. One of the largest studies of GSM and UMTS base stations was performed in Bavaria in Germany, and showed that the median level was at 1.2% of the ICNIRP guidelines with the maximum emission being 0.072 mW/cm^2 (corresponding to 7.8% of the ICNIRP guidelines).[15] Studies have shown that using distance from a base station as a surrogate of exposure is inaccurate. As the antenna does not radiate uniformly, there is a main lobe with side lobes of RF and null areas. As many base stations are located well above ground level, the areas immediately adjacent to the base station may be in null areas, such as the case with a study where the lowest power density levels from a base station installed 30 m above ground were at 80 m and highest levels of power density were at 230 m from the station.[15] Better predictors of exposure are orientation of the main lobe and line-of-sight conditions.[16]

5.3.4 Wireless Local Area Networks (WLAN)

WLAN allows devices to connect wirelessly with a central hub. WLAN has a maximum transmission power between 100–200 mW and primarily operates at 2.4–2.4835 GHz, although some operate at 5.15–5.825 GHz. "Terminals" consist of laptop computers and other devices and the point of entry to the wired network is an "access point" usually located within tens of meters of the terminals in the same building.[2] Wireless Fidelity (WiFi) networks, which are types of WLAN, transmit bursts or "pulses" of RF.[12] Worldwide Interoperability for Microwave Access communication technology (WiMAX) is essentially a larger version of a WiFi network. Through the use of orthogonal frequency division multiple access (OFDMA), it operates on a larger scale with multiple overlapping access points and has a range of many square miles.

With the small size of antennas inside laptops and other WiFi devices the distance to the far field (where exposure attenuates rapidly) is relatively short.[2] For example, if the antennas are 5–10 cm in size, radiating near field extends to no more than 16 cm at 2.4 GHz and 33 cm for 5 GHz.[2]

Although, WLAN antennas would ideally radiate omnidirectionally, often they radiate in certain directions with nulls in others. Therefore, the extent to which the radiated power is directed toward a user is useful for understanding exposure. One study showed that antennas in laptops are oriented such that most of the RF irradiates along the screen and up away from the body.[2] Most WiFi devices have several antennas which allow for switching of individual bursts to the appropriate antenna for optimal

performance. Due to the different locations of antenna in the device, the radiation pattern can change depending on which antenna is in use.[2]

For WLAN devices, the duty cycle increases when data are transmitted and depends on the rate of data transmission.[2] Even when no data are being transmitted, the access point transmits a signal (beacon) lasting 0.5 ms every 100 ms to allow devices to synchronize with it.[11] For transmission of a beacon, the average output power is 0.5 mW, but for a large amount of data, the mean output power can be up to 70 mW.[11] For the same data rate, however, a higher order of modulation (more bits encoded per symbol) reduces the duty cycle, leading to lower exposure. In addition, maximum data rates can be achieved when WiFi devices are close to the access point, but rates fall with increasing distance, being affected by reflections from surrounding objects and network congestion.[2]

Field strengths are higher from access points compared to terminal devices. In the Peyman et al. study (2011),[2] the field strength of the access points was almost double that of the laptops. In a study of SAR for access points and PC,[11] values were 0.27 and 0.11 W/kg, respectively, using the Institute of Electrical and Electronics Engineers (IEEE) WLAN g standard (the most common WLAN standard used today).[43]

WLAN hotspots are areas where internet access is available, such as in airports or stations. Access points are usually mounted in ceilings or walls and rarely in floors. The energy emitted from these hotspots has been measured to be much lower than ICNIRP's recommended maximum level of 61 V/m (1 mW/cm^2).[11]

5.3.5 Smart Meters

Smart Meters record consumption of electricity, water, and natural gas and transmit information wirelessly to the utility company for billing purposes.[44] A number of different wireless technologies can be used, including CDMA, LTE and WiFi.[1] There are different types of Smart Meters. Most transmit in the 900 and 2.4 GHz frequency bands and communicate with a utility access point that can be located on transmission line poles that are high above ground or, in the case of a mesh network, at a central residence.[13,44] Smart Meters transmit data several times a day for milliseconds at a time,[13,44] therefore the duty cycles are quite low (0.07% to a peak of 4%).[7,14,44] A number of studies have been conducted measuring the power density of Smart Meters utilizing different assumptions of duty cycle and output power (Tables 1 & 2).

One recent study measured the output power of Smart Meters in a mesh network, which consisted of 500 and 750 residences through which data was transmitted to a single residence collection point that then relayed the network data to the utility. Three different types of transmitters were evaluated: 1) RF Local Area Network (LAN) at 900 MHz which interconnects residences, 2) Home Area Network (HAN) at 2.4–2.5 GHz which interacts with devices and equipment within a residence, and 3) a cell relay (GSM 900 MHz or CDMA 1900 MHz) that serves as the mesh network's collection point,

which relays data to the utility.[13] The study differed from previous studies on Smart Meters in that the output power immediately at the surface of the meter was ascertained and no duty cycle was assumed. The authors indicated that readings at the meter surface brought the probe's protective shell into contact with the meter within the reactive near field of the meter antenna which may have led to inaccurate high readings. Even if measurements were inaccurately high, the 99.5th percentile of measurements at the face of the Smart Meters were lower compared to the nominal peak output power of mobile phones (398 mW vs. 2W for GSM at 900 MHz and 115 mW vs. 250 mW for CDMA at 1900 MHz).[13] At 20 cm from the meter, the levels dropped by about 10-fold in most cases.[13] Most other studies conducted their measurements at various distances from the meter and assumed various duty cycles.[7,14,44]

5.3.6 Microwave ovens

Microwave ovens work in the 2.4 GHz band at an output power of between 500–2000 W. A study on 60 new appliances measured an average leakage of 0.08 mW/cm^2. For used appliances, the leakage from three studies (with a total of 339 appliances ranging in age from 0.1 to 23 years) was < 0.062 (for 50% of ovens), 0.17 (average), and 0.41(average) mW/cm^2.[18-20] Worn or dirty door seals, or work door or catch were the more likely causes of leakage RF. In one study of SAR, researchers prepared the microwave oven to leak at the maximum permitted level and measured SAR at 30 cm (whole body exposure) and 5 cm (equivalent to head exposure). The levels were 0.0056 W/kg and 0.256 W/kg, respectively. The only time that ICNIRP recommended levels were exceeded was when the body made direct contact with the operational microwave with doors closed (7.95 W/kg).[40]

5.3.7 Bluetooth

Bluetooth allows for high-frequency (2.4 GHz) voice and data transfers over short distances. For example, it can connect a headset wirelessly to a mobile phone or a laptop to a printer. Bluetooth devices are categorized into three power classes. Most of the Bluetooth devices that come in contact with the body are Class 2 and 3, which are weak and limited in range. Some Bluetooth transmitters are in Class 1, which allows access to the internet and can produce power levels similar to mobile phones. The maximum transmission power of Class 1 is 76 mW compared to 1.9 and 0.8 mW for Class 2 and 3, respectively.[11]

When Bluetooth devices with the same communication profile are in the same area, they automatically communicate with each other. Up to eight devices can link in what is known as a piconet. There is one device that is known as the master (which takes the lead and organizes the data transfer) and the other devices are "slaves." Time slots are assigned to devices, but if several time slots are combined, then the pulse frequency drops to 533 Hz (for three time slots) and 320 Hz (for five time slots). If no data transfer is occurring, the slaves do not transmit but receive a beacon from the master

periodically. Since Bluetooth devices switch on and off, they only consume power when transferring data. This produces low frequency magnetic fields of about 1 Hz (beacon) up to several thousand.[11]

Blue tooth devices which transmit in the frequency band of 2.4–2.5 GHz emit RF at a hundred times lower than mobile phones.[42] SAR was measured for two different Bluetooth Universal Serial Bus (USB) plug-in antennas in Class 1 and 2 at maximum data rate and maximum output power, one Class 2 personal digital assistant (PDA), and two different hands-free headsets. SAR levels ranged from 0.00117 to 0.466 W/kg (Table 2).[11] At 20 cm, the electrical field decreased rapidly to about 20–150 times lower than ICNIRP standards (1 mW/cm^2).[11]

5.3.8 Broadcasting

Analogue FM radio and TV broadcasting antennas operate at frequencies from 80 to 800 MHz, and the antennas have output power of 10 to 50 kW. The total power of the newer digital video (DVB) and audio (DAB) broadcasting systems is lower than that for analogue broadcasts. The highest power DVB-T transmitter has an average effective radiated power (ERP) of 200 kW per multiplex, as opposed to the analogue version with 1000 kW ERP per service. While the DAB channel transmitter has an ERP of up to 10 kW, the main VHF FM transmitter ERP is 250 kW per service.

5.3.9 Other RF sources

Wireless mice and keyboards of PCs operate at 20–40 MHz frequency range, lower than other wireless systems; RF is emitted when moving, clicking or typing with the devices.

Baby monitoring systems consist of a baby unit and one or two parent units and operate at a variety of different frequency bands (between 27 to 2400 MHz), which correspond to power and range. Parent units are primarily receivers, but some can transmit and receive. Certain systems have a video monitor, which requires transmission at 2400 MHz. Most baby monitors do not transmit continuously but only when certain sound levels are reached. Some systems test that the parent unit is within range by sending out test signals every few seconds. The SAR for two baby monitors at frequencies of 863 MHz and 446 MHz transmitting at 10 mW and 500 mW were 0.01 and 0.08 W/kg, respectively (Table 2).[11]

Radio-controlled toys such as cars and gliders operate at different frequencies and output powers vary widely. Similarly, RF identification technology such as road tolling and security cards range in frequencies up to 5.8 GHz.[1]

Other personal effects such as metal accessories (including jewellery) can also affect conductivity of RF waves, but based on engineering principles the effect is small.[21]

Natural sources of exposure to RF include the sun, which emits low power densities of less than 0.001 mW/cm^2.[45] Our own bodies emit RF fields from approximately 30 to 300 GHz at 0.0003 mW/cm^2.[46]

5.3.10 Area exposure measurements

Joseph et al. (2012)[47] conducted 30-minute area measurements in 311 locations in three European countries (Belgium, The Netherlands, and Sweden) using a narrowband spectrum analyzer. The average electric field strength for all sources was low at 0.71 V/m (equivalent to 0.000134 mW/cm^2) with GSM 900 and GSM 1800 sources dominating (0.49 and 0.24 V/m, respectively). Higher total values were obtained outdoors compared to indoors because field strengths of mobile phones were not assessed in the study. LTE, UMTS with High Speed Packet Access (HSPA) and DECT and FM were comparable (0.017, 0.16, 0.15, and 0.15 V/m, respectively). In indoor environments, even though DECT results are the second highest (after GSM 900), authors caution that exposures to DECT were overestimated as uplink (mobile phone to base station) traffic was also measured at this frequency band. Average electric field strength for WMAX, which was only available in a few cities in Belgium and The Netherlands, was 0.07 V/m compared to 0.03 V/m for WLAN. LTE and WiMAX are relatively new and not as common as GSM.[47]

5.3.11 Personal Exposure Measurements (PEM)

Real-life exposure measurements from multiple sources have been attempted using personal exposure meters for frequency selective exposure assessment. One study measured source exposures and personal exposures using exposimeters on 166 participants in Basel, Switzerland.[48,49] The mean weekly personal exposure to all RF sources was 0.013 mW/cm^2 when measurements during personal phones calls were excluded and 0.015 mW/cm^2 when they were included.[49] The greatest contributors were mobile phone base stations, mobile phones, and DECT cordless telephones. Mean values were highest in trains, airports, and tramways or buses, and higher in the day than at night.[48]

Viel et al. (2009)[50] conducted personal exposure measurements (PEM) of 377 people in France for 24 hours. The total field mean value was 0.201 V/m (equivalent to 0.0000107 mW/cm^2) with the greatest contributor being FM sources (0.044 V/m), followed by similar readings for WiFi, UMTS mobile phones and cordless phones. Levels were higher in the daytime for GSM uplink (communication from mobile phone to base station) and Digital Cellular Service (also known as GSM 1800) downlink (base station to mobile phone), whereas levels for Tetrapol (walkie-talkies), TV and UMTS were higher during the sleeping hours. The total field was higher outdoors than indoors, which was due to transportation contributing most to the total PEM.[50]

Joseph et al. (2008)[33] conducted PEM for five hours for each of 28 different realistic exposure scenarios (combinations of outdoors/indoors, rural/urban, standstill/moving, night/day) in Ghent, Belgium. The highest outdoor exposures were due to downlink signals of GSM and DCS (up to 0.52 V/m or 0.0000717 mW/cm^2). The authors noted that high indoor exposure can occur from WiFi (up to 0.58 V/m) and DECT (up to 0.33 V/m). Outdoor scenarios with highest maximum values were GSM DL (downlink) and indoors were lower as the signals had to penetrate through building materials. The highest total exposure occurred for train and bus scenarios due to GSM UL (uplink) (up to 1.90 V/m or 0.000959 mW/cm^2) and DCS UL (uplink) (up to 0.44 V/m) exposures, particularly at night. The higher number of handovers from GSM and DCS and higher concentration of people likely meant that more uplink communication was occurring. During the day (outdoors), mostly FM, GSM DL, and DCS DL were present. At night, GSM UL, DCS UL, and DECT were much lower while WiFi was present both day and night with the highest levels at night. FM, TV/DAB, TV, and GSM DL did not differ much when comparing day and night in a fixed location. Fewer RF sources were available in rural Belgium (e.g., UMTS was not yet deployed), therefore exposures were generally lower for the investigated scenarios. Joseph et al. calculated whole body SAR using the PEM data; for instance, for an electric field value of 0.26 V/m, they calculated the higher limit, p95 (SAR), to be 2.08 μW/kg and for 0.36 V/m they calculated it to be 3.88 μW/kg, which are close to one hundred thousand times below exposure limits.[33]

A 24-hour RF exposure profile was collected of 3022 children and adolescents in four Bavarian cities in Germany.[51] Half of the children and nearly all of the adolescents owned mobile phones which were used for short durations during the day only. The data were expressed as a mean percentage of the ICNIRP standards; the overall exposure was very low and ranged from a mean of 0.13% to 0.92% of the ICNIRP reference level per second during waking hours.[51] Authors did not report levels separately for each of the different frequency ranges that were covered (GSM 900 and 1800 up and downlink; and WLAN).

One study by Joseph et al. (2010)[52] attempted to compare PEM across countries in Europe—Belgium, Switzerland, Slovenia, Hungary, and the Netherlands—using the same personal exposure meters. The highest exposure occurred in transportation vehicles (trains, cars, buses), particularly during uplink of mobile phones with three frequency bands of 880–915 MHz, 1710–1985, and 1920–1980 MHz (range of 0.0000239 to 0.000101 mW/cm^2). DECT phone measurements were much lower than for mobile phones but were greatest in office and urban homes (primarily in the range of 0.000 to 0.000006mW/cm^2). FM measurements ranged up to 0.0000096 mW/cm^2 and were higher than for TV/Digital Audio Broadcasting and WLAN. WLAN measurements were highest in the office and urban home (0.000 to 0.0000018 mW/cm^2). Tetrapol, WLAN and TV/Digital Audio Broadcasting (DAB) were considered minor sources of RF.

A recent study by Bolte and Eikelboom (2012)[53] in the Netherlands was able to discern through the additional use of a GPS logger, the spatial and temporal differences in RF exposure for 98 people (excluding their own phone calling) over 24-hour exposure periods. The mean power density was 0.000018 mW/cm^2, with evening exposure being about four times higher than nighttime and twice as high as daytime. The main contributor to exposure was other people in the vicinity making calls from mobile phones and DECT phones. The activities contributing most to exposure included ones occurring in places with a high density of people, such as travelling using public transportation, and at social events, pubs and shopping malls. The highest peak exposure in the WiFi band was 0.0265 mW/cm^2 from use of a microwave for a short period of time.

5.4 Discussion

The public is exposed to RF from several sources on a daily basis. For the most part, exposure assessment studies have found all RF levels from sources to be below current exposure limits (the limits are provided in Section 13). The highest exposures result from being in the near-field of active RF devices, with personal use of a mobile phone at the head contributing most to total RF exposure. Because cordless phones do not exhibit power control like mobile phones, they can potentially emit more RF than UMTS mobile phones, although they do emit less than GSM mobile phones. WLAN devices emit far less RF than mobile phones and cordless phones but may be used for longer periods of time. Power densities near WLAN access points are greater than WLAN terminals. In general, being in the far-field of sources, such as the case with base stations and broadcast stations results in far lower exposures than using RF-emitting devices in the near field.

Personal Exposure Measurement (PEM) data are often dominated by RF from mobile phones, DECT phones, and WLAN, but surprisingly FM has been found to contribute substantially to far-field exposures.[50] Overall, exposures are higher in the daytime due to higher usage of mobile phones and cordless phones; however, WiFi sources are prevalent both day and night.[47] Being in transit produces higher exposures with personal use of GSM mobile phones (which produce maximum output power upon each handover). Also, in mass transit, such as in buses or trains, other passenger use of wireless devices contributes to personal exposure.[52] However, ambient exposure from others' use of WiFi and mobile phones contributes much less to exposure than personal usage of a RF device.

Total PEM tend to be higher in rural locations, likely due to a lower density of mobile phone base stations. Although intuitively, one may assume that an increase in base stations means higher ambient exposure, mobile phones do not need to use as much power (due to adaptive control) to communicate with the base stations due to shorter distances. As a good connection translates into lower output power levels, urban centres with higher base station densities often experience lower RF than rural centres.

The nominal peak output power levels of WLAN and Smart Meters are comparable to some mobile phones (e.g., 250 mW), but the duty cycle of these systems are low, meaning that these systems do not transmit often or for extended periods of time. In addition, these devices are not meant to be used in the near field (at the head or body) and therefore exposure decreases with distance from the source.

Although mobile phones and wireless communication systems contribute most to overall personal exposure, with each generation of mobile phones, the RF that is emitted is lower due to changing technologies and higher base station densities. Although 3G technologies like UMTS produce lower output power levels than previous generations, GSM (2G), which has unique features that result in higher output power levels, is still being used in current 3G and 4G model phones that have the capability of switching from one technology or frequency to another. For instance, new mobile phones using LTE or WiMax technologies will fall back to GSM or CDMA networks when 4G networks are unavailable.[54] Therefore, knowledge of output power characteristics of 2G technologies remains important for understanding contributions to current personal exposure.

5.4.1 Limitations

There are many new and emerging sources of RF for which very little exposure information is available. One study of area measurements evaluated LTE and WiMax, but indicated the difficulties with exposure assessment given that these networks were not well established in these areas.[47] In addition, other uses of RF such as for aesthetic purposes (e.g., RF facials) have been documented in the literature, but as of yet, no exposure studies have been conducted.

In reviewing exposure data from various studies, it is not possible to directly compare study exposure measurements to each other as study parameters differ substantially. Studies are conducted in different locations and use different sampling techniques, sampling intervals, sampling equipment, distances, and models of RF-emitting devices. Even within the same study, output power can vary substantially depending on location of study centres and network operators.[24,32] However, comparisons of different devices within each study can be used to determine relative output power. Measurement of power density, electric fields, and SAR are all subject to limitations in measurement accuracy.

As there has been public concern over pulsed modulated waves, a research gap is an absence of assessment of pulsed modulation. Some studies compared devices with pulse modulation to those without and one study conducted measurements at intervals that were sufficiently small to capture the pulsing of GSM phones.[8] Most studies assumed a cumulative exposure model in devising their sampling strategies for comparison with current standards, but this biological model may not be appropriate. A reasonable alternative is a rate of change model which assumes that the frequency of RF oscillates from higher intensity to lower intensity in a particular RF event. When undertaking exposure assessment studies, researchers must ensure that their

sampling protocol is sufficient to capture the salient features of the chosen model (for instance, ensuring that the sampling interval is sufficiently short to capture any peaks, so that peaks are not averaged out in a long sampling period when applying a repetition model).

In order to determine exposure from all sources, some knowledge of the individual contributions of sources must be considered. However, it is difficult to assess exposure from multiple sources that emit at similar frequencies (e.g., microwave oven and WLAN), and for PEM, researchers must rely on accurate activity logs to distinguish one source from another.

Also, PEM indicates a field value close to the human experience but the user's exposure is dependent on how the device is used. For instance, a mobile phone can be used at the head or with a headset with the phone in a pocket or purse. Since the monitors are usually hung at the waist, they do not capture actual exposures from sources held close to the body at different locations.[50] In addition, PEMs are appropriate for capturing far-field exposures, but are inappropriate for measuring near-field exposure. As a result, PEMs may underestimate true exposure.

5.4.2 Future implications

As with mobile phones, we expect that each generation of new technologies of RF-emitting devices will become more energy-efficient and therefore produce lower average output power. However, there is a growing demand that new technologies handle more data and transmit it more quickly, thereby possibly increasing the power necessary to handle the demand. LTE and similar technologies enabling high data rate applications will increase; these new and emerging technologies will create new exposure scenarios that will require assessment.[15]

In addition, the duration of exposure to sources of RF is increasing with time, so future exposure assessment studies must consider the duration as well as type of use of various devices. Average ambient exposure levels to RF measured in urban areas of the US in 1975 were 0.005 mW/cm^2; in 1998 the exposure levels were 0.05 mW/cm^2 in Sweden, and in 2009 the averaged power density in Greece urban areas was 0.39 mW/cm^2. Differences in methodology and location affect direct comparison, but the trend of increasing exposure to RF is evident. In 1975 the principal sources of RF were from broadcast band signals, whereas more than 60% of RF exposure is presently attributed to wireless telecommunication devices.[55]

Although ideally it would be preferable to capture personal exposure information in future studies, PEM studies that collect total field measurements from all RF sources for all subjects can be resource-intensive, therefore some researchers have investigated methods for predicting field exposures without doing PEM. A modest correlation (R^2 of 0.56) was shown between PEM and questionnaire data coupled with RF measurements from fixed site transmitters to predict personal RF exposure.[48] Also,

another study evaluated the correlation between measured source data and modelled data for a city and rural area and found good correlation for different types of sources including mobile phones and broadcast stations.[9] Dose phones (software modified phones) have been used consistently to measure GSM power control levels which can be proxies for actual output power levels. These dose phones have shown good correlation with GSM source measurements[8]; therefore, there may be potential in creating dose phones using newer generation models of phones that could easily be used by participants in future studies.

In future studies, it may be important to measure the pulse power density in addition to the average power density. More research is needed to determine a biologic marker of exposure.

As for SAR compliance testing, a recent study showed that peak temperature increase was a better metric for detecting localized heating effects of RF and suggests that peak temperature increase for a specific duration of exposure be used instead of the current restrictions based on SAR 10 g or 1 g.[56]

5.5 Conclusion

Due to the widespread use of RF devices, average exposure of the general public above natural background levels is increasing but remains much lower than internationally accepted guidelines. The greatest contributor to personal exposure to RF is use of mobile phones at the head. The output power levels in the near field of RF devices are hundreds to millions of times higher than ambient field levels. Although the intensity of exposure for most RF emitting devices is below any current exposure limits and becoming lower over time for mobile phones, there are also more sources for which we have very little exposure measurement information. Also, duration of exposure is increasing to the many different sources of RF; therefore, it continues to be necessary to assess individual sources of exposures and total exposures over time.

Summary of Factors that Affect RF Power Density

1. **Technology.** The type of technology contributes the most to power variation of mobile phones. Mobile phones using CDMA technology emit the least RF. There is little research yet on 4G phone technologies.

2. **Antenna configurations.** Often RF antennas do not radiate omnidirectionally, but instead radiate in certain directions with nulls in others.[2] Knowing the direction of the main lobe will help inform the general public of placement of RF-emitting devices or in locating mobile phone base stations.

3. **Adaptive control.** For most mobile phones, the network exercises power control or adaptive control, which reduces RF power of each roaming unit to a minimum level compatible with voice quality for a conversation.[21] Therefore, mobile phones usually transmit at less than maximum power.

4. **Duty cycle.** The duty cycle is the ratio of pulse duration to the pulse repetition period and applies to technologies that pulse, such as with GSM or WiFi. Depending on the duty cycle, the average output power levels will differ (e.g., average powers will be much higher with duty cycles of 100% vs. 1%).

5. **Distance.** In the far field, power density is inversely proportional to the square of the distance. However in the near field, close to the RF-emitting device, this relationship does not apply. Also, shorter distances between a receiver and access point or base station reduces the output power necessary to communicate. For instance, a higher density of mobile phone base stations means that the output power levels of mobile phones will be lower than for lower density areas.

6. **Frequency.** Radio waves penetrate less into body tissues as frequency increases[2]; therefore, people will absorb less RF from devices using higher frequency bands.

7. **Data rates and signal quality**. Data transfer causes higher output power than voice.[10] Good signal quality reduces output power.

8. **Location.** Whether an RF device is being used indoor vs. outdoors or in a rural vs. urban location will affect exposure.

9. **Transit**. Being in a moving vehicle tends to increase average output power levels. Much of the increase can be attributed to GSM mobile phones switching base stations, but for mass transit, it can also be attributed to the number of wireless devices being used by passengers.

10. **Size.** A larger antenna will increase the size of the near-field. Also, size of the person being exposed will affect exposure. For the same emitted power, children and fetuses experience higher SAR.

11. **Models of RF devices.** Different models of RF devices produce different output power levels and can be affected by size of antenna, antenna placement, packaging, etc. However, the differences between models of mobile phones are small compared to differences between technologies.[8,24]

12. **Tissue type.** The amount of reflection, absorption and transmission from specific RF frequencies varies with the type of material and its thickness. RF at telecommunication frequencies generally tend to be absorbed and may penetrate into the body tissues for a few centimetres.[1]

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5.7 Appendices

Appendix A: Equations Related to Exposure

1. dBm – referenced to 1 mW
2. dBm = 10 log [Signal (mW)/1mW]
3. Power (mW)=10^dBm/10
4. λ = c/f; where λ is the wavelength, c is speed of light 3x10E8 m/s, and f is the frequency in Hz (cycles/second)
5. Reactive near field = λ/2π; where λ=wavelength
6. Boundary between near and far field: d = 2 L^2/λ; where d=distance; L=length of antenna; λ =wavelength
7. **To convert mW/m^2 to mW/cm^2 divide by 10,000**
8. **To convert mW/cm2 to W/m2 multiply by 10**

Section 6

Biological Effects of Radiofrequency Exposure

Section 6A Cell Culture Studies

Table of Contents

Summary

- Use of cell culture models to investigate effects of environmental exposures can lead to elucidation of biologic mechanisms to explain adverse effects which help direct animal and human health research. Many cell culture studies have recently (2005–2012) been published to assess whether radiofrequency (RF) field exposure has adverse biological effects on a variety of cells.
- Studies of DNA damage and RF field exposure at non-thermal levels using indicators such as chromosomal aberrations and micronucleus have shown mixed results, with a few positive studies and many negative ones. There is no convincing evidence from cell culture studies that RF field exposure damages DNA.
- There is no evidence from recent cell culture studies that exposure to RF fields alone can induce transformation. Results of studies concerning the effect of RF fields on cell proliferation when RF fields are applied alone is mixed, with a few positive studies showing decreased proliferation with exposure to RF but many negative studies as well. More research is needed on the effect of RF fields in conjunction with known carcinogenic exposures such as ionizing radiation.
- Evidence of the presence of reactive oxygen species (ROS) or of apoptosis (cell death) in cell cultures due to exposure to RF fields is contradictory, with some studies showing evidence of generation of ROS or of apoptosis and others none. Recent studies on each of these putative study outcomes have been well conducted and no particular aspect of the study protocols characterize positive versus negative studies.
- Recent well conducted studies of the effect of RF fields in induction of ornithine decarboxylase (affecting tumour growth) have been predominantly negative, even under conditions of cell stress or stimulation.
- The question of whether non-thermal RF fields induce changes in expression of heat shock or other genes or proteins is open, as the results of studies are quite contradictory. However, as in most other aspects of cell culture research, there are no specific frequencies or characteristics (pulsed or continuous wave) of RF exposure which distinguish positive from negative studies.
- A variety of physiologic processes in neurologic and other cells have been tested under exposure to RF fields, with no weight of evidence to indicate that such RF exposure adversely affects any process.
- There is little evidence from recent studies that RF fields adversely affect calcium channelling in cultured cells.

- There have been only a few studies recently assessing the effect of RF fields on cell cultures designed to mimic the blood-brain barrier, and these are mostly negative. Most of the work in this area has been recently conducted using animal models.

- Overall, in spite of the many well-conducted cell culture experiments examining a number of putative effects from RF fields, there is no convincing evidence that exposure to such fields has adverse biological effects. In many areas of research, the results are inconsistent and contradictory. The lack of features distinguishing positive studies from negative ones has prevented the development of any credible biologic mechanism by which such fields might adversely affect cells in culture.

6A.1 Introduction

Over the past 25 years, many studies have been conducted to determine whether RF field exposure can have adverse effects on human health, but in spite of the effort, there is still much uncertainty. Studies of the putative relationship between RF exposure and chronic diseases such as brain cancer carried out in humans are observational in nature rather than experimental. Most observational studies are retrospective in nature and consequently provide incomplete information on RF exposure and a lack of control of confounding variables, which complicates the process of determining cause and effect. In addition, a significant period of time elapses between exposure and subsequent disease, making causal relationships more difficult to establish.

Experimental studies under laboratory conditions allow manipulation of exposure and measurement of effect. Human-derived cell and tumour lines are plentiful, outcome measures can be achieved quickly, and biological processes known to be involved in chronic disease can be studied under controlled conditions. If such studies show that RF fields initiate or promote biological processes known to be involved in chronic disease, and these results are independently replicated by other researchers, then this can lead to development of testable biological mechanisms to better understand and predict effects of RF. Although cellular studies cannot determine the interactions between cells seen in living systems, biologic mechanisms suggested by cell line studies can then be rapidly tested in experimental animal models. Thus, studies in cell lines can play a key role in advancing knowledge about the possible relationship between RF exposure and human disease.

6A.2 Purpose

The purpose of this review is to summarize the recent literature (2005–2011) on the effects of RF fields on cell cultures which are most relevant to possible adverse human health effects. A few *a priori* limitations were established. First of all, it is well known that RF fields at high power can cause thermal effects, including stimulation of heat-shock proteins, alterations in DNA, and in extreme cases, cell destruction. However, the fields to which humans are exposed in day-to-day use of RF devices do not cause

any notable heating, and thus studies involving changes due to thermal effects were not included. Near field intensity of RF fields within cell cultures or tissue is described by the metric specific absorption rate (SAR) measured in "watts per kilogram" of tissue. SAR values under realistic day-to-day conditions of use from RF sources rarely exceed levels of about 2 W/kg in humans, and consequently studies which examine the effects in vitro and animal model studies that generate SAR levels around or below these levels will be emphasized whenever possible.

Further, as the major human concern to date with RF fields concerns use of cellular or mobile phones, the review will concentrate largely on studies of the frequencies between 800 MHz and 2450 MHz, as these are the commonly used frequencies in North American, Asian and Nordic telephony at the present time. Although use of the latest generation of RF devices using the Long Term Evolution (LTE) standard and marketed as 4G is rapidly expanding, little information on its effect on biologic systems is available at this time.

6A.3 Methods

A search of the online databases PubMed (MEDLINE), and EBSCO Academic Search was conducted using search terms "radiofrequency field," "radiofrequency radiation," "RF radiation," "microwave," "cellular phone," "mobile phone," and these key words were combined with terms for carcinogenesis, genotoxicity, DNA damage, chromosome(al) aberration, micronucleus formation, apoptosis, gene expression, ornithine decarboxylase, cell permeability, protein expression, gene expression, cell proliferation, and cell transformation. The search was restricted to peer-reviewed articles published in English since 2005 to 2011. After eliminating duplicate references picked up by multiple searches, there were 126 studies found for more detailed review. A separate search using the term "WiFi" linked to cancer, and various other terms including "health" produced only one genuine in vitro investigation. Review articles were separated out so bibliographies could be searched; and recent national reviews of RF fields and health such as the Latin American Experts Committee on High Frequency Electromagnetic Fields and Human Health report[1] and the UK Health Protection Agency's recent report[2] were also examined for papers missed by other means.

Although this review will concentrate mainly on more recent studies (2005–2011), summary paragraphs at the end of each group of potential adverse biological effects will consider all available evidence and not just included studies published since 2005. The reason for the emphasis on more recent work is that these investigations are more likely to be characterized by good RF dosimetry and better experimental protocols offering good control of the potential confounding effect of thermal changes. Sometimes, earlier investigations will be referenced to provide context for study of a particular adverse effect.

Within each category of in vitro biological effects on cells, a representative group of studies were chosen for tabular presentation and discussion. These studies are, for the

most part, characterized by good experimental methods, accurate RF dosimetry, use of RF frequencies that humans are exposed to on a day-to-day basis (such as GSM and CDMA mobile phone frequencies), and SAR values of around 2 W/kg.

6A.4 Cancer-Related Effects

To facilitate conduct of in vitro studies, blood lymphocytes, buccal, skin or other cells can be obtained from human volunteers or animals. In addition, cancer or other cells may be extracted from humans or animals, immortalized using a virus or other means, and cultured, forming cell lines. Such cell lines remain genetically constant over time and can be used for years to produce "test cells" for many studies. Thus, investigators seeking to repeat an experiment done by another scientist can use the same cell line as used in a previous study with reasonable assurance that the test cells are genetically very similar to the original.

A sham group refers to cells which are grown in exactly the same conditions and undergo all the manipulations that the RF-exposed cells go through except for the RF exposure itself. This helps ensure that other conditions of the experiment do not cause cellular changes which might then falsely be attributed to RF field exposure. Including a positive control group can also be a valuable addition to an experiment as it provides a standard against which changes in the experimental cells can be compared.

6A.4.1 DNA damage and RF fields (Table 1)

One of the principal concerns with RF fields is whether they have the ability to cause cancer alone, or to promote cancer in the presence of other known carcinogens. Since damaged DNA is characteristic of cancer cells, indications of damage due to RF field exposure are important. DNA damage is manifested in a number of ways in cells, including chromosomal aberrations, micronucleus formation, and DNA strand breaks. Chromosomal aberrations occur when a cell divides, and this process does not take place properly. Micronucleus formation occurs when a daughter cell inherits an incomplete complement of chromosomes plus a small micronucleus carrying the whole or partial chromosome missing from the actual nucleus. Chromosomal aberrations and micronucleus formation are characteristics of genetic instability and are associated with diseases such as cancers.

Vijayalaxmi (2006)[3] at the University of Texas Health Sciences Centre extracted lymphocytes (while blood cells) from blood samples collected from non-smoking male donors and exposed the samples to pulsed 2450 MHz or 820 MHz RF fields or sham for two hours at SAR levels of 2.3 W/kg or 20.7 W/kg. Another group of lymphocytes was exposed to an acute gamma radiation exposure of 1.5 G, known to cause DNA damage, and was maintained as a positive control group. Cultured lymphocytes were then examined to determine the extent of cytogenetic damage incurred with the RF exposure. No differences were seen in percentage mitotic index, chromosomal exchange aberrations, or excess fragments in the RF-exposed cells by comparison with

sham- exposed cells. As expected, the positive control cells showed elevated damage levels compared to both sham- and RF-exposed cells. The investigator concluded that the results showed no indications that RF field exposure increased DNA damage by comparison with sham exposure.

Stronati et al. (2006)[4] exposed lymphocytes from 14 healthy donors to 935 MHz basic GSM signal (SAR 1.0 and 2.0 W/kg) or sham for 24 hours either alone or combined with one- minute exposure to 1.0 Gy of 250 kVp x-rays given either immediately before or after RF exposure. Results showed no elevation in DNA strand breakage, chromosomal aberrations, sister chromatid exchanges, or micronucleus formation in the RF-field-exposed cells by comparison with sham-exposed cells. In addition, RF exposure did not enhance DNA damaging effects in the x-ray exposed cells.

A further study in fibroblasts by Speit et al. (2007)[5] used V79 hamster fibroblasts exposed to 1800 MHz continuous wave RF fields or sham exposure on an intermittent schedule (5 minutes on, 10 off) for 1 to 24 hours. The RF exposure was performed in a temperature-controlled wave guide chamber (SAR of 2.0 W/kg). Positive and negative control cultures were also included in the protocol. Evaluation after exposure using the Comet assay showed no increase in DNA damage in the RF-exposed cells compared to the sham-exposed and control groups. The Comet assay is a test in which RF-exposed cells are lysed in an agarose gel and exposed to pulsed electrophoresis. The lysed cell material, when observed using fluorescent microscopy, appears like a comet, and DNA damage is assessed by the size of the comet "tail." In addition, the study did not detect any increased micronucleus formation, another indication of DNA damage, in the RF-field-exposed cells.

Mazor and his colleagues (2008)[6] exposed lymphocytes from 10 volunteers to a continuous wave RF field at 800 MHz or sham in a wave-guide resonator at SARs of 2.9 and 4.1 W/kg for 72 hours. The study was conducted over a range of temperatures from 33.5 to 40.0ºC to evaluate the contribution of thermal effects to any changes observed. Assessment of the lymphocytes after exposure at 37ºC showed increased aneuploidy in chromosomes 1 and 10 at the higher SAR, and in chromosomes 11 and 17 at the lower SAR level, indicating damaged DNA in the RF-exposed cells. Aneuploidy is an abnormal number of chromosomes and occurs when chromosomes do not separate properly at cell division. Elevated levels of aneuploidy were also seen at other temperatures, leading investigators to conclude that elevated damage levels in RF-exposed cells might be independent of temperature.

In a further study, conducted by Manti et al. (2008),[7] lymphocytes were exposed to x-rays (4 Gy) known to cause DNA damage, and subsequently to 1950 MHz UMTS signal at 0.5 or 2.0 W/kg SAR or to sham exposure for a period of 24 hours. Analysis revealed a small but statistically significant increase in the amount of DNA damage per cell in cells exposed to x-rays and 1950 MHz signal at a SAR of 2.0 W/kg compared to those exposed to x-rays and sham RF exposure. The authors suggested that this might be

evidence of an inhibiting effect exerted by RF fields on cells' DNA repair mechanism following damage by x-rays.

The study of Zeni et al. (2008)[8] evaluated peripheral lymphocytes (circulating white blood cells) from healthy volunteers to exposure for 24–68 hours to intermittent 1950 MHz RF fields (six minutes RF on; two hours off; SAR 2.2 W/kg) or sham in a transverse electromagnetic cell (TEM). The protocol included temperature control measures as well as negative and positive control (mitomycin-C; methylmethanesulphonate exposure) cells. Results of comet and micronucleus assays showed no effects on DNA structure and no increase in micronucleus formation or changes in cell cycle kinetics attributable to RF field exposure.

Schwarz and colleagues (2008)[9] exposed human-cultured fibroblasts to 1950 MHz UMTS signal (SAR below 2 W/kg) for 8, 12, or 24 hours in a commercial incubation chamber with good control of temperature. Results showed increased micronucleus formation and enhanced comet tail factor response in cells exposed for 24 hours at SAR 0.5 W/kg, indicating DNA damage.

Kim et al. (2008)[10] exposed L5178Y mouse leukemia/lymphoma cells to 835 MHz CDMA signal in a TEM cell at 4.0 W/kg or sham for 24 or 48 hours. At Comet assay, no increase in chromosomal aberrations were seen in the exposed cells in comparison with the sham exposed cells; however, in conjunction with the clastogenic agents cyclophosphamide or 4-nitroquinoline 1-oxide, which are known to produce chromosomal damage, RF exposure appeared to potentiate the damage brought about by these agents. The relevance of this study to human health issues is questionable as the SAR level is much higher than is seen in day-to-day use of RF devices.

With Sannino et al. (2009),[11] human dermal fibroblasts were exposed to 900 MHz pulsed GSM signal for 24 hours (SAR 1.0 W/kg) alone and in conjunction with the potent mutagen 3-Chloro-4-(dichloromethy)-5-Hydroxy-2(5h)furanone (MX). Comet assay results revealed no genotoxic or cytotoxic damage from RF field exposure alone or enhanced DNA damage due to the addition of RF exposure to MX.

In a further similar study, Hansteen et al. (2009)[12] collected blood from six healthy donors, separated and cultured their lymphocytes, and exposed the cultured lymphocytes to 2300 MHz pulsed or continuous wave signal or sham in an anechoic chamber, alone or in conjunction with mitomycin C, a known clastogen. A clastogen is a compound known to cause chromosomal breaks. Field intensity was given to be 10 W/m^2 although no SAR levels are noted. Results showed no differences in either damaged DNA in RF- exposed cells alone, compared with sham-exposed, and in addition no enhanced damage or slower DNA repair in those exposed to mitomycin C and RF fields, in comparison with sham and mitomycin C.

Campisi et al. (2010)[13] exposed rat astroglial cells to 900 MHz continuous and pulsed GSM signal for 5, 10, or 20 minutes at a SAR of 0.25 W/kg and showed increased DNA

damage as indicated by Comet assay results in RF cells compared to sham-exposed and control cells. In addition, the RF-exposed cells showed increased production of reactive oxygen species (ROS) by comparison with control cells.

Table 1. Genotoxic DNA damage and RF fields in cellular studies

Study	Cell Type	Exposure	Results	Comments
Vijayalaxmi (2006)[3]	Human lymphocytes	2450 MHz or 820 MHz pulsed fields; 2.1 or 20.7 W/kg for 2 hrs	No difference in DNA damage in RF cells compared to controls	Positive control group exposed to gamma radiation included in study
Stronati et al. (2006)[4]	Human lymphocytes	935 MHz signal; SAR 1.0 and 2.0 W/kg for 24 hrs	No DNA damage from RF exposure	
Speit et al. (2007)[5]	V79 hamster fibroblasts	1800 MHz continuous wave; intermittent exposure SAR 2 W/kg	Comet test negative; no micronuclei	
Mazor et al. (2008)[6]	Human lymphocytes	800 MHz continuous wave exposure or sham; SAR 2.9 or 4.1 W/kg for 72 hrs	Increased aneuploidy in RF-exposed cells compared to sham- exposed	Conducted at temperatures of 33.5–40ºC.
Manti et al. (2008)[7]	Human lymphocytes	4 GY x-ray exposure +1950 MHz UMTS signal SAR 0.5 or 2.0 W/kg for 24 hrs or sham	Burden of x-ray induced chromosomal damage enhanced by RF exposure at SAR 2.0 W/kg	Authors proposed RF exposure may inhibit DNA repair
Zeni et al. (2008)[8]	Human lymphocytes	1950 MHz intermittent exposure; 2.2 W/kg for 24– 68 hrs	No chromosomal aberrations or micronucleus formation	
Schwarz et al. (2008)[9]	Human fibroblasts	1950 MHz UMTS signal; SAR < 2.0 W/kg or sham exposure for up to 24 hrs	Increased micronucleus formation; +ve Comet assay	
Kim et al. (2008)[10]	Mouse leukemia-lymphoma cells	835 MHz CDMA signal; 4.0 W/kg up to 48 hrs	No chromosomal aberrations with RF exposure alone	RF exposure appeared to enhance effect of clastogenic agents

Study	Cell Type	Exposure	Results	Comments
Sannino et al. (2009)[11]	Human dermal fibroblasts	900 MHz pulsed GSM signal SAR 1.0 W/kg for 24 hrs and MX mutagen	Comet assay showed no enhancement of MX-induced DNA damage by RF exposure	
Hansteen et al. (2009)[12]	Human lymphocytes	2300 MHz pulsed signal at 10 W/m^2 for 53 hrs or sham, with and without Mitomycin C	No chromosomal differences in RF cells compared to controls either with or without Mitomycin C	No SAR levels found in paper
Campisi et al. (2010)[13]	Rat astroglial cells	900 MHz continuous and pulsed for 5, 10 or 20 min; SAR 0.25 W/kg	Comet test showed increased DNA damage in RF- exposed vs. sham and control cells	Production of ROS in RF exposed cells

Summary

For direct indicators of DNA damage such as chromosomal aberrations and micronucleus formation, the evidence for an effect of RF fields alone among cell cultures is not strong, largely because studies show such inconsistent results. For instance, among fibroblast cell culture studies, the investigations of Schwarz et al.[9] showed DNA damage but that of Speit et al.[5] did not. A comprehensive review of data by an expert group under the aegis of the International Agency for Research on Cancer concluded that for most end points in cell culture studies including DNA damage, studies of low intensity (non thermal) RF exposure provided only weak evidence of any effect.[14] Adding to the difficulties of making sense of the contradictory results seen is the fact that most recent studies use first-rate cell culturing techniques, well-validated measures of DNA damage, excellent temperature control to rule out thermal effects, and well-described RF exposure protocols.

6A.4.2 Cell transformation and proliferation and RF fields (Table 2)

Cell transformation is an important step in the process of carcinogenesis, involving escape of a clone of cells from contact inhibition, by which cells surrounding the clone restrict its ability to proliferate. Cell proliferation in normal healthy cells is restricted to a rate commensurate with the function of those cells within the cellular matrix they are growing in. Although the process of carcinogenesis results in an increased rate of proliferation in cells, in normal routinely growing cultures proliferation can be an indication of cell stress.

There have only been two recent studies involving the effect of RF field exposure on cell transformation since 2005, and both have been negative. Wang et al. (2005)[15] exposed mouse C3H10T1/2 fibroblasts to continuous wave 2450 MHz electromagnetic fields at specific absorption rates of 5 to 200 W/kg for two hours in conjunction with methylcholanthrene, a known initiating chemical, or to methylcholanthrene alone. The transformation frequency of cells was slightly increased with the addition of 2450 MHz exposure, but only at SAR levels in excess of 100W/kg—almost 100 times as high as seen in normal human exposure to RF fields.

A Japanese study (2008)[16] exposed BALB/3T3 mouse cells to 2142 MHz W-CDMA signal at SAR of 80 and 800 mW/kg for six weeks alone and in addition to 3-methylcholanthrene, and also on RF-exposed cells initiated with MCA and co-exposed to TPA. Results showed no significant increase or decrease in transformation frequency and no promotion effect resulting from RF exposure. Both these results confirmed negative cell transformational findings from an earlier 2001 investigation.[17]

Studies of the ability of RF fields to affect cell proliferation rates have been more frequent, with more than 30 conducted since 2006, although fewer than half used human cells.

The study of Miyakoshi et al. (2005)[18] exposed MO54 human glioma cells to 1950 MHz continuous wave RF exposure at SARs of 1, 2, and 10 W/kg or sham in a temperature controlled incubation chamber for 10, 30, 60, or 120 minutes. Results indicated that RF exposure had not altered proliferation rates of the cells in comparison with sham-exposed cells.

Italian study investigators (2007)[19] exposed SH-SY5Y cells from a human neuroblastoma cell line to pulsed 900 MHz fields at a SAR level of 1 W/kg or sham for periods of 5, 15, or 30 minutes, or 6 or 24 hours in an isothermal incubator. Cells RF exposed for 24 hours showed a transient increase in Egr-1 gene (a key transcriptional factor gene) expression and impaired cell cycling, with G_2M accumulation, indicating a halt in cell cycling and a slowing in cell proliferation as well as onset of apoptosis, as indicated by down regulation of the Bcl-2 gene.

Proliferation studies have also been carried out using other cell types including fibroblasts. Pavicic and Trosic (2008)[20] exposed V79 Chinese hamster fibroblasts to 864 MHz continuous wave RF signal at SAR of 0.08 W/kg, or 935 MHz RF field at 0.12 W/kg in a transverse electromagnetic field cell (TEM cell) for one, two or three hours, along with positive and negative controls, and showed decreased proliferation in the cells exposed to RF fields for two or three hours. No effect however, was seen on cell viability or colony forming ability due to RF exposure. This group of investigators showed similar results in another study[21] also conducted in 2008.

Investigations using similar scientific protocols, but conducted in other labs using fibroblasts, did not show the same effects. Hoyto et al. (2008)[22] exposed L929

fibroblasts to 872 MHz continuous wave or pulsed GSM signal at a SAR of 5 W/kg for 1 or 24 hours with or without menedione (to induce production of reactive oxygen species) or tert-butylhydroperoxide (to induce lipid peroxidation, the oxidative destruction of fats) along with completely unexposed control cells. At analysis, the L929 cells exposed to pulsed but not to continuous wave RF fields, and menedione showed some increase in caspase-3 activity. Caspase-3 is a protein that plays a role in induction of apoptosis, the process of programmed cell destruction. However, in L929 cells exposed exclusively to any form of RF exposure alone, no effects at all including levels of caspase-3 activity or of cell proliferation were seen compared to control cells. In the same experiment, SH-SY5Y cells, (a human neuroblastoma cell line) were also exposed to the same RF fields as well as menedione or tert-butylperoxide. In this cell line, no changes in either cell proliferation or in caspase-3 induction were seen with application of RF fields alone or in conjunction with either of the oxidants.

A further study by the same investigator exposed L929 fibroblasts to pulsed 872 MHz RF fields (SAR 5 W/kg) in a waveguide chamber.[23] However, during the experiment, the investigators also added a change of cell culture medium (known to increase proliferation) to the protocol to see if the RF exposure might further increase the expected rise in proliferation expected from the culture medium change. After exposure of 1 hour or 24 hours to RF fields, measurement of proliferative activity was assessed at 24 and 48 hours, and no significant differences were seen between cells exposed to RF fields, as well as a medium change by comparison with cells exposed to the medium change only.

Lee et al. (2008)[24] exposed NIH3T3 mouse fibroblasts to 849 MHz signal at SAR levels of 2 or 10 W/kg or sham for either one hour or one hour per day for three days in an exposure chamber maintained isothermally using a circulating water jacket. After RF or sham exposure, cells were transferred to an incubator, and cell proliferation rates were measured 24 and 48 hours later. No significant difference was detected in proliferation rate between the RF-exposed and sham-exposed cells.

Cao and colleagues (2009)[25] exposed SHG44 human glioma cells to 900 MHz or sham in an EMCO chamber two hours a day for three days. On day four, the cells were exposed or sham-exposed to 5 Gy gamma radiation at a dose rate of 1 Gy/minute. At the conclusion of the study, pre-exposure with 900 MHz fields prior to gamma radiation exposure appeared to enhance the decrease in cell proliferation induced in cells treated with gamma radiation, although in the groups of cells treated with RF alone, little difference was seen compared with control cells unexposed to either gamma radiation or RF fields. Cells exposed to RF and gamma rays also showed increased reactive oxygen species (ROS) compared with those exposed to gamma radiation alone, but the expression of hsp70 (heat shock protein) remained unaltered.

A Japanese study (2010)[26] exposed two types of cells of human neurologic origin (A-172 glioblastoma; H4 neuroglioma) to continuous wave 2142 MHz W-CDMA signal at

SARs of 80, 250 and 800 mW/kg or sham in anechoic chambers for up 24, 48, 72, or 96 hours and found no change in cell proliferation due to RF exposure.

Table 2. Cell proliferation and RF field exposure in cellular studies

Cell Transformation				
Study	**Cell Type**	**Exposure**	**Results**	**Comments**
Wang et al. (2005)[15]	C3H10TI1/2 mouse cells	Methylcholanthrene alone or with 2450 MHz continuous wave signal; SAR levels 5 W/kg to 200 W/kg or sham for 2 hrs	Transformation with addition of RF field exposure increased slightly only at SAR levels of > 100 W/kg	SAR levels much higher than experienced by humans
Hirose et al. (2008)[16]	BALB/3T3 mouse cells	2142 MHz W-CDMA signal; SAR .08 or .8 W/kg or sham alone or with methylcholanthrene or alone and with TPA for 6 wks	RF fields up to 0.8 W/kg does not induce or co-promote cell transformation	

Cell Proliferation				
Study	**Cell Type**	**Exposure**	**Results**	**Comments**
Miyakoshi et al. (2005)[18]	MO54 human glioma cells	1950 MHz IMT-2000 signal SAR 1–10 W/kg for 1–2 hrs	No change in cell proliferation compared to non-RF- exposed cells	
Buttigione et al. (2007)[19]	SH-SY5Y neuroblastoma cells	900 MHz pulsed field; SAR 1.0 W/kg or sham for 24 hrs	Impaired cell cycle with decreased proliferation	Apoptotic cells seen after 24 hrs
Pavicic and Trosic (2008a)[20]	V79 fibroblasts	864 MHz continuous wave; SAR .08 W/kg or 935 MHz continuous wave signal; SAR 0.12 W/kg for 1, 2, or 3 hrs or sham	Decreased cell proliferation rate in cells after 2–3 hrs RF exposure	Colony forming ability and cell viability not affected by RF exposure

Cell Proliferation				
Study	**Cell Type**	**Exposure**	**Results**	**Comments**
Pavicic and Trosic (2008b)[21]	V79 fibroblasts	864 MHz or 935 MHz continuous wave SAR 0.08 at 864 and 0.12 W/kg at 935 for 1, 2, or 3 hr controls	Decrease in proliferation 72 hrs post RF exposure vs. control cells	
Hoyto et al. (2008a)[22]	L929 fibroblasts	872 MHz continuous or pulsed GSM signal; SAR 5 W/kg , with or without menedione or tert-butylhydroperoxide for 1 or 24 hrs or sham	No change in cell proliferation in RF-exposed compared with control cells	
Hoyto et al. (2008b)[23]	Murine L929 fibroblasts	872 MHz continuous or pulsed signal; SAR 5W/kg or sham for 1 or 24 hrs	No change in cell proliferation 48 hrs after exposure	Slight increase in ODC activity but thought to be chance finding
Lee et al. (2008)[24]	NIH3T3 mouse fibroblasts	849 MHz CDMA signal; SAR 2 or 10 W/kg or sham for 1 hr only or 1 hr on each of 3 days	No alteration in cell proliferation 24 or 48 hr after RF exposure vs. control cells	
Cao et al. (2009)[25]	SH 44 human glioma cells	900 MHz at 2, 4 or 6 W/cm, 2 hrs/day for 3 days; with or without γ radiation on day 4	Exposure of cells to 900 MHz prior to γ radiation enhanced decrease in proliferation vs. no RF	No SAR given. RF alone had no effect on proliferation vs. sham exposure alone
Sekijima et al. (2010)[26]	H4 neuroglioma cells and A172 glioblastoma cells	2142 MHz continuous wave W-CDMA SAR 80, 250, 800 mW/kg or sham up to 96 hrs	No change in cell proliferation in RF-exposed vs. unexposed cells	No change in gene expression in exposed vs. unexposed cells

Summary

There is no convincing evidence that radiofrequency fields alone can induce transformation in cell culture studies. There is a lack of consistent results concerning cell proliferation in cells of human neurologic origin in these studies that characterizes the state of knowledge in cells of all types in this area. Positive results are usually not replicated. The finding of Cao et al.[25] suggesting that pre-exposure to RF fields prior to exposure to gamma radiation, potentiates the cell cycling effects of ionizing radiation however, does merit follow-up studies. Studies of the ability of RF fields to alter proliferation in other types of cells such as keratinocytes, melanoma cell lines and in prokaryotic yeast, and bacterial cells have produced conflicting results, in the same fashion as seen in cells of neural origin or fibroblasts. Although the recent studies are in general of good quality with excellent cell culturing protocols well-established end point assays and good RF dosimetry, it is difficult to draw conclusions as to whether RF fields affect proliferation in any kind of animal or human cell. The results do not support the emergence of any plausible biologic mechanism which might explain altered proliferation due to RF fields.

6A.4.3 Apoptosis and RF fields (Table 3)

Apoptosis, or programmed cell death is a natural process in which cells which have undergone damage which cannot be repaired, particularly DNA damage, are eliminated by being engulfed by phagocytes rather than undergoing necrosis which would spread cell contents and initiate inflammation throughout the body. In cells which are becoming malignant due to irreparable genetic damage, apoptosis is considered positive; however, the presence of significant apoptosis in normal cell lines is generally indicative of cellular damage.

German investigators, Lantow et al. (2006),[27] exposed human cultured monocytes (Mono Mac 6 cells) to 1800 MHz GSM-DTX fields with a SAR of 2 W/kg or sham in a CO_2 incubator alone or in conjunction with gliotoxin or phorbol-12-myrystate-13 acetate (PMA) for 12 hours. Gliotoxin is known to increase apoptosis, and PMA is a chemical which increases necrosis. The incubator assisted with temperature control and provided a chamber to ensure accurate RF dosimetry. After 72 hours, examination of the cells exposed to RF fields alone showed no difference in indicators of apoptosis by comparison with the sham exposed cells. In addition, RF exposure did not increase apoptosis levels in gliotoxin treated cells by comparison with sham-exposed cells treated with gliotoxin. RF exposure alone or in conjunction with PMA also did not increase necrosis levels by comparison with sham and sham +PMA treated cells.

Joubert and colleagues in France (2006)[28] exposed human neuroblastoma SH-SY5Y cells to 900 MHz continuous wave (SAR 2 W/kg) or pulsed (0.25 W/kg) RF exposure or sham at either 37 or 39°C for 24 hours, and after assessing an increase in apoptosis using three methods, showed no significant alteration in RF-exposed cells by comparison with sham-exposed.

Another study by the same team (2007)[29] exposed cultured rat neuronal cells to 900 MHz GSM signal at SAR levels of .25 W/kg or sham for 24 hours in an incubator. Assessment of apoptosis was carried out immediately after RF exposure and at 24 hours post exposure using three different methods including evaluation of caspase-3. None of the three test methods gave an indication of increased apoptosis in RF-exposed cells compared to sham-exposed cultures. A positive control using the same rat cells exposed to staurosporine for three hours at 37˚C was also included in this study.

Zhao et al. (2007)[30] evaluated whether expression of genes related to apoptosis were dysregulated in cultured mouse neuron cells and astrocytes by exposure to 1900 MHz GSM mobile phone signal for two hours. An actual mobile phone was placed over the cultured cells for exposure, so SAR levels were not available. Gene array analysis showed up-regulation of caspase-2 and caspase-6 in neurons in both the "on" and "stand-by" phone modes but only in the "on" mode in astrocytes. An actual SAR value was not noted in the publication, and illustrations in the paper showed exposure of cells in culture dishes using an open flip-top mobile phone placed over the dishes. It should be noted that this type of exposure using an actual mobile phone that does not yield a homogeneous RF field and may interfere with temperature control.

In a study using continuous wave rather than pulsed RF fields at 900 MHz (SAR 2 W/kg) Joubert and her French team (2008)[31] again evaluated whether exposure for 24 hours would induce apoptosis in rat neurons by comparison with sham exposure. Although no increase in caspase-3 activity (an indicator of apoptosis) was seen with RF exposure, a significant increase was seen in another measure of apoptosis; namely apoptosis inducing factor (AIF), a flavoprotein which initiates a non-caspase-related apoptotic cascade by causing DNA fragmentation.

Moquet et al. (2008)[32] studied the effect of exposure to 935 MHz GSM basic, GSM talk or continuous wave unmodulated signal (compared to GSM pulsed signals) or sham for 24 hours on murine N2a neuroblastoma cells. A set of positive controls (exposed to 4 Gy x-rays) was included in the protocol. Three different assays (Annexin V, caspase activation, in situ end-labelling) were used to evaluate indications of apoptosis, but no differences were seen between any type of RF exposure and sham-exposed cells.

Palumbo and colleagues (2008)[33] investigated the induction of apoptosis in quiescent and proliferating human peripheral lymphocytes (white blood cells) after exposure to 900 MHz GSM RF radiation or sham. The exposure was carried out at an average specific absorption rate of 1.35 W/kg in a dual wire patch cell exposure system where the temperature of cell cultures was accurately controlled. After one hour exposure to the RF field, a slight but statistically significant increase in caspase-3 activity, measured six hours post-exposure was observed in proliferating human PBLs (22%). In contrast, no effect was detected in quiescent human PBLs.

Other cell lines such as leukemia, human fibroblasts, and mouse stem cells also showed mixed results for indications of apoptosis due to RF field exposure.

The study of Hoyto et al. (2008)[22] noted above exposed SH-SY5Y neuroblastoma cells and mouse L929 fibroblasts to a continuous wave of pulsed 872 MHz fields for 1 or 24 hours, either alone or in conjunction with menedione, or tert-butylhydroperoxide. Results showed an increase in caspase-3 activity in the L929 cells but no increase in the SH-SY5Y cells by comparison with similarly treated sham groups.

A further study by the same investigators (2008)[23] exposed murine L929 fibroblasts to 872 MHz pulsed or continuous wave RF fields at a SAR of 5 W/kg or sham for 1 or 24 hours and found no increase in caspase-3 activity in either short-term or long-term RF exposed cells compared to their respective sham groups.

Table 3. Apoptosis and exposure to RF fields in cellular studies

Study	Cell type	Exposure	Results	Comments
Lantow et al. (2006)[27]	Human Mono Mac 6 cells	1800 MHz GSM-DTX signal; SAR 2 W/kg for 12 hrs or sham; alone or with gliotoxin +PMA	No increased apoptosis (or necrosis) in monocytes exposed to RF fields alone or with gliotoxin +PMA	
Joubert et al. (2006)[28]	SH-SY5Y human neuroblastoma cells	900 MHz GSM pulsed or CW signal; SAR .25 or 2 W/kg or sham for 24 hrs at 37 and 39ºC	No increased indications of apoptosis in RF-exposed cells	
Joubert et al. (2007)[29]	Cultured rat neuronal cells	Pulsed 900 MHz GSM signal; average SAR 0.25 W/kg for 24 hrs or sham	No indications of increased apoptosis in RF-exposed cells compared to sham- exposed	
Zhao et al. (2007)[30]	Cultured mouse neurons and astrocytes	1900 MHz GSM signal for 2 hrs from a phone in “stand-by” or “on” modes	Up regulation of caspase-2 and 6 genes in RF exposed cells	SAR not available as actual mobile phone placed over culture dishes was used for RF exposure

Study	Cell type	Exposure	Results	Comments
Joubert et al. (2008)[31]	Cultured rat neuronal cells	900 MHz CW signal; SAR 2 W/kg; 24 hrs at 37 or 39ºC or sham	Indications of apoptosis through AIF pathway at 37 and 39ºC in RF-exposed cells compared to sham	
Moquet et al. (2008)[32]	Murine neuroblastoma cells	935 MHz in GSM basic, talk or CW signal; SAR 2 W/kg, for 24 hrs or sham	No indication of increased apoptosis in RF-exposed cells	
Palumbo et al. (2008)[33]	Human peripheral lymphocytes	900 MHz GSM signal; SAR 1.35 W/kg for 1 hr or sham	Increased caspase-3 in proliferating but not quiescent PBLs	
Hoyto et al. (2008a)[22]	L929 fibroblasts and SH-SY5Y neuroblastoma cells	872 MHZ CW or pulsed GSM signal; SAR 5 W/kg , with or without menedione or tert-butylhydroperoxide for 1 or 24 hrs or sham	Increased caspase-3 in L929 cells with menedione + RF exposure	No increase in caspase-3 seen in SH-SY5Y cells
Hoyto et al. (2008b)[23]	Murine L929 fibroblasts	872 MHz continuous or pulsed signal; SAR 5 W/kg or sham for 1 or 24 hr	No differences in caspase-3 in RF-exposed vs. sham-exposed cells	Slight increase in ODC activity but thought to be chance finding

Summary

Studies of apoptosis in human cell lines, cultured monocytes, and fibroblasts provided conflicting evidence of apoptotic activity resulting from pulsed or continuous wave RF exposure. Very similar protocols, even with the same investigative teams, appear to provide conflicting results. With few exceptions, recent studies are well-conducted and do not provide evidence of a single factor or constellation of factors which are associated with whether study results will be positive or negative. The current state of knowledge does not provide any consistent support for the theory that RF fields increase apoptotic activity in any given cell type.

6A.4.4 Reactive oxygen species and RF exposure (Table 4)

Reactive oxygen species (ROS) form naturally in normal cell physiological processes involving oxygen; however, when cells are under stress due to adverse environmental conditions (for example, heat or ionizing radiation), more may be formed than can be scavenged by antioxidants. While low levels of ROS have a role in physiologic processes such as apoptosis, high levels can cause damage to cell structures, and because ROS contain free radicals, they can damage DNA.

European investigators (2007)[34] exposed L929 murine fibroblasts to either 900 MHz continuous wave or 900 MHz GSM pulsed signal for 10 or 30 minutes at SAR rates of 0.3 and 1.0 W/kg or sham with or without co-exposure to sub-toxic levels of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX), a mutagen and carcinogen produced in chlorination of water. When MX was used, RF exposure followed within 10 or 30 minutes afterward. Formation of reactive oxygen species (ROS) was monitored and ROS harvested until one hour after RF exposure. Results indicate that ROS production in cells exposed to RF fields alone was not significantly different from sham cells. In addition, by comparison with MX and sham-exposed cells, RF field exposure did not enhance formation of reactive oxygen species known to take place in the presence of MX.

Cao et al. (2009)[25] in a study mentioned earlier, exposed SHG44 human glioma cells to gamma radiation (5 Gy over five minutes) with or without 900 MHz RF field exposure of two hours per day for six days. No increase in oxidative stress levels as indicated by increased levels of superoxide dismutase (SOD) or malondialdehyde (MDA) were seen with RF exposure alone by comparison with control cells. However, enhanced formation of reactive oxygen species (elevated SOD and MDA) were seen when RF field exposure preceded gamma radiation exposure by comparison with levels seen with ionizing radiation alone.

Brescia et al. (2009)[35] exposed immortalized human lymphoblastoid T-cells (Jurkat cells) to 1950 MHz UMTS (3 G) signal or sham at SAR levels of 0.5 or 2 W/kg for time periods between 5 and 60 minutes (short-term exposure) or 24 hours (long-term exposure). Concurrent studies were carried out with cells exposed to both ferrous sulphate (known to induce ROS) and RF fields, to see if RF exposure enhanced the reactive oxygen species levels induced by $FeSO_4$. No change in cell viability consistent with increased ROS production was seen for cells exposed to RF fields alone compared to sham-exposed cells, and no enhanced ROS effect was seen in the iron-exposed cells.

Chinese investigators, Xu et al. (2010),[36] exposed cultured cortical neurons to 1800 MHz pulsed fields at SAR 2 W/kg or sham, for a period of 24 hours to determine whether exposure caused an increase in reactive oxygen species which might damage mitochondrial DNA in cells. Another group of cells were exposed to hydrogen peroxide to provide a positive control for reactive oxygen species production, and a further group was exposed to melatonin four hours prior to administration of RF exposure. Analysis 24 hours post-exposure showed increased indications of ROS formation, including increased levels of 8-hydroxyguanine, decrease in the copy number of mitochondrial DNA and decreased levels of mitochondrial RNA transcripts. Interestingly, cells exposed to melatonin, a potent antioxidant, prior to RF exposure showed no increase in ROS.

Campisi et al. (2010)[13] exposed cultured astroglial cells isolated from newborn rats to 900 MHz carrier wave or amplitude modulated RF fields for 5, 10, or 20 minutes at 10 V/m. A significant increase in ROS levels and DNA fragmentation was seen in cells exposed to amplitude-modulated fields for 20 minutes but none for shorter periods. No effect was seen with continuous wave exposure for any of the three time periods. The investigators hypothesized that the positive effect of increased ROS levels for modulated RF exposure might be due to hyperstimulation of glutamine receptors in the brain. The authors also noted that the observed increase in ROS levels might be modified in vivo by neural repair mechanisms.

Table 4. Reactive oxygen species and RF field exposure in cellular studies

Study	Cell Type	Exposure	Results	Comments
Zeni et al. (2007)[34]	L929 mouse fibroblasts	900 MHz continuous and pulsed GSM signal; SAR 0.3 or 1.0 W/kg for 10 or 30 min + MX (mutagen)	No ROS increase with RF alone; no increase with RF exposure over MX level and sham	
Cao et al. (2009)[25]	SHG44 human glioma cells	900 MHz GSM signal at power density of 2,4, or 6 mW/cm^2 for 2 hrs/day for 6 days with or without 5 Gy γ radiation	RF exposure increases ROS over that seen with γ radiation alone. No increase in ROS with RF exposure alone	
Brescia et al. (2009)[35]	Jurkat cells	1950 MHz UMTS signal (SAR 0.5, 2.0 W/kg) or sham for 5-60 min or 24 hrs, with or without $FeSO_4$	No increase in ROS from RF alone. No enhancement of ROS in $FeSO_4$ treated cells	
Xu et al. (2010)[36]	Cortical neurons	1800 MHz pulsed signal; SAR 2 W/kg; or sham for 24 hrs, with and without prior melatonin exposure	Increased production of ROS in exposed cells. No increase when RF preceded by melatonin	
Campisi et al. (2010)[13]	Rat astroglial cells	900 MHz amplitude modulated or CW fields; power density .26 W/m or sham for 5, 10, or 20 min	Increase in ROS levels and DNA fragmentation	No SAR given

Summary

Recent studies of RF exposure and production of reactive oxygen species show both positive and negative results. There is no consistent evidence from cellular studies that a specific type of cell is more or less susceptible to increased ROS formation under conditions of RF field exposure alone. Some but not all studies have indicated that RF exposure might enhance production in conjunction with administration of agents known to increase ROS in cells. More research is needed in this area.

6A.4.5 Ornithine decarboxylase activity and RF fields (Table 5)

Ornithine decarboxylase (ODC) is a key enzyme which is activated in polyamine biosynthesis. Polyamines are essential for cell growth and proliferation, and cancers have higher levels of polyamines than normal tissue. Activation of ODC is thought to be associated with tumour promotion and progression. This has increased interest in whether exposure of cells to RF fields results in activation of ODC.

An American study, Penafiel et al.,[37] conducted in 1997 exposed mouse L929 cells to analogue and digital 835 MHz signals. The RF signals in the study were produced using analogue and digital mobile telephone, and the authors noted that uniformity of electrical fields over the cells in growth flasks may not have been uniform. The analogue fields produced a 90% transient increase in ODC levels that peaked at eight hours after RF exposure and disappeared by 24 hours post exposure, and a TDMA pulsed digital signal produced a 40% increase. Continuous wave exposure produced no change in ODC levels. Results of this study must be treated with caution due to potential problems with RF dosimetry.

More recent studies of the effect of RF field exposure using more modern exposure methods and research protocols are available.

Hoyto et al. (2006)[38] evaluated the effects of RF fields and changes in temperature on ODC activity in L929 fibroblasts in an attempt to confirm the results of the Penafiel study.[37] After exposure to pulsed or continuous wave 900 MHz GSM signal in an aluminum RF resonator at SAR levels of 0.2 or 0.4 W/kg for 2, 8, or 24 hours, the RF-exposed cells showed no increase in ODC activity by comparison with sham-exposed cells. The investigators noted in the course of the study that an increase in temperature of less than 1ºC did produce an increased level of ODC activity. This study did not confirm the results of Penafiel et al.[37] but did suggest that ODC was very sensitive to changes in temperature in the cell culture.

In a similar study carried out in 2007 with a more extensive variety of cell lines, Hoyto et al.[39] exposed L929 fibroblasts, rat C6 glioblastoma cells, human SH-SH5Y neuroblastoma cells, and rat primary astrocytes to 872 MHz pulsed or continuous wave RF fields at SAR levels of 1.5, 2.5, or 6.0 W/kg or sham exposure for 2, 8, or 24 hours. L929 cells, rat C6 glioblastoma cells and SH-SH5Y cell types showed no elevation in

ODC activity with RF exposure for 2, 8, or 24 hours by comparison with sham-exposed cells. However, rat primary astrocytes showed significantly decreased levels of ODC with exposure levels of 1.5 or 6.0 W/kg using pulsed or continuous wave exposure. The authors noted that since the activity levels of primary astrocytes were likely to be closer in response to living tissue, and as these cells showed decreased ODC activity, the results did not support the theory that RF field exposure increased ODC levels.

Hoyto and her colleagues[23] conducted a further study searching for possible alterations in ODC levels in cells exposed to RF fields. The authors hypothesized that stressing cells by serum deprivation, or stimulating cells by the addition of fresh culture medium, might change their ODC response to RF fields. As in previous studies, L929 fibroblasts were exposed to 872 MHz pulsed or continuous wave RF exposure or sham in a waveguide exposure chamber at a SAR of 5 W/kg for 1 or 24 hours, with and without the addition of fresh culture medium and with or without serum deprivation. ODC levels assessed at 1 and 24 hours showed slight increases in levels after RF exposure in cultures either stressed from serum deprivation or stimulated with fresh medium, by comparison with sham-exposed cultures similarly treated. However, only one of the 15 slightly increased levels was statistically significant, and the authors concluded that the one significant increase was a chance result due to multiple testing. They concluded that stressed and stimulated cells were not more sensitive to RF field-induced ODC effects than cells in a normal metabolic state.

A French study, Billaudel et al. (2009)[40] exposed L929 fibroblasts to 835 MHz pulsed Digital Advanced Mobile Phone System (DAMPS) signal, 900 MHz or 1800 MHz pulsed GSM or sham for eight hours with a SAR level of 2.5 or 6.0 W/kg in an attempt to replicate the findings of Penafiel et al.[37] The different RF exposures were carried out in appropriate vessels with fans to control temperature at the high SAR levels under which the experiments were conducted. The investigators found no alterations in ODC activity in RF-exposed cells at any of the test frequencies by comparison with sham-exposed cells and concluded that the results did not support the earlier findings of the American study.[37]

Table 5. Ornithine decarboxylase activity and RF field exposure in cellular studies

Study	Cell Culture	Exposure	Results	Comments
Hoyto et al. (2006)[38]	Murine L929 fibroblasts	915 MHz pulsed or CW signal; SAR 0.2 or 0.4 W/kg or sham for 2, 8, or 24 hrs	No increase in ODC with pulsed or continuous wave RF exposure	Increase in temperature of 0.8°C produced increase in ODC activity
Hoyto et al. (2007)[39]	Murine L929 fibroblasts; rat C6 glioblastoma cells; human SH-SH5Y glioblastoma cells; rat primary astrocytes	872 MHz GSM pulsed or CW signal; SAR 1.5, 2.5, or 6.0 W/kg for 2, 8, or 24 hrs or sham	No increase in ODC levels with RF in any cells except rat primary astrocytes where ODC levels decreased with pulsed or CW RF exposure	
Hoyto et al. (2008b)[23]	L929 fibroblasts	872 MHz pulsed or CW signal; SAR 5W/kg for 1 or 24 hrs or sham ± stimulation with fresh culture medium± serum deprivation	Cells responded to medium change and to serum deprivation as expected. No significant increase in ODC activity in stressed or stimulated cells with RF exposure	
Billaudel et al. (2009)[40]	L929 cells	835 MHz pulsed DAMPS signal; or 900 MHz or 1800 MHz pulsed signal SAR 2.5 W/kg for 8 hrs	No increased ODC activity for any of the RF- exposed cell cultures	

Summary

Results from recent well conducted studies appear to indicate that no increase in ODC activity results from either pulsed or continuous wave RF field exposure. Further, even under conditions of cell stress or stimulation, very little or no increase in ODC levels are seen with RF field exposure.

6A.5 Gene Expression and RF Fields

Gene expression is the process by which the information genes carry is used to make RNA and protein products. Most genes produce copies of themselves called RNA transcripts; proteins are made using these transcripts as instructions. A gene can be up-regulated or down-regulated at the DNA level (by causing the gene to produce more (or less) RNA transcripts) or at the RNA level (by stabilizing the transcript so that it can make more (or less) protein molecules). Some genes are expressed quite uniformly with little variation over time, routinely producing proteins to maintain the normal functions of the cell, while expression of other genes can be induced or repressed by signals that depend on external stimuli from agents either alone or in combination with other factors. Several studies recently have been conducted evaluating the effect of RF fields on a number of genes. These are described in two categories, namely studies of expression of heat shock genes and proteins, and studies of other types of genes and protein expression changes.

6A.5.1 Heat shock gene and protein changes and RF fields (Table 6)

One of the most commonly used indicators of cellular stress in RF health research is the alteration in expression of heat shock genes or proteins. Heat shock proteins are involved in the folding and unfolding of other proteins and have been highly conserved throughout evolution. They act as intra-cellular chaperones, moving other proteins around and preventing polypeptide chains from aggregating into non-functional structures. Heat shock protein levels increase in conditions of environmental stress such as excess heat, inflammation, and exposure to toxins. Their up-regulation is considered part of a generalized stress response on the part of a cell, and this is why they have been used extensively in RF research. Indications of increased or reduced synthesis of proteins can also be useful as measures of cell stress under adverse environmental conditions, and a number of studies have focussed on heat shock proteins. Many early studies showing heat shock protein changes with RF exposure have had inadequate control of RF heating,[41] but more recent studies have been better designed.

Czyz et al. (2004)[42] exposed p53 deficient and wild type embryonic stem cells to 1710 MHz pulsed RF fields at SAR levels of 0.4 to 2.0 W/kg or sham intermittently (5 minutes on and 30 minutes off) for between 6 and 72 hours in hanging drops and in suspension. Results showed an up-regulation of heat shock protein Hsp70 in the p53 deficient differentiating cells but not in wild type cells.

Miyakoshi and other Japanese investigators[18] exposed MO54 human glioma cells to 1950 MHz continuous wave RF exposure at SARs of 1, 2, and 10 W/kg or sham in a temperature controlled incubation chamber for 10, 30, 60, or 120 minutes. No altered expression levels were seen for Hsp27 or Hsp70 heat shock proteins in RF-exposed cells by comparison to sham-exposed cells.

Wang and colleagues (2006)[43] studied the effect of exposure of A172 human glioblastoma cells on expression levels of heat shock genes Hsp70 and Hsp27. Cells were subjected to 2450 MHz RF fields at SAR levels of 5 to 200 W/kg or sham for one to three hours in an incubator. As exposure at high SAR levels is likely to cause temperature increases in culture medium, appropriate heat control cell groups (38–44˚C) were incorporated into the protocol. Results showed no changes in expression levels of Hsp70 or Hsp27 at 5 W/kg, a level much higher than seen in day-to-day human use of RF devices. However, it may induce a transient increase in Hsp27 phosphorylation in the A127 cells at SAR levels greater than 100 W/kg, although such high levels have no relevance to normal human exposure.

Sanchez et al. (2006)[44] in France evaluated the effect of 900 MHz pulsed signal at a SAR of 2 W/kg for 48 hours on the expression of Hsp70, Hsp27, and Hsc70 in human isolated keratinocytes and in human reconstructed epidermis (hRE). No change was seen in any of the gene expression parameters in isolated keratinocytes following RF exposure, but at three weeks and again at five weeks, slight but significant increases in Hsp70 expression was seen in the hRE, although there were no changes in hRE thickness or in proliferation, suggesting the gene expression change has no functional effect. The authors interpreted the results as indicating that exposure to 900 MHz RF fields was unlikely to have adverse effects at the human skin level.

Chauhan et al. (2006)[45] in Canada exposed human lymphoblastoma cells to 1900 MHz pulsed RF fields at SAR levels of 1 and 10 W/kgor sham for periods of five minutes on exposure, 10 minutes off for six hours. Evaluation of levels of Hsp70 expression and Hsp27 expression were assessed and no significant differences were seen between RF-exposed cells and sham-exposed cells.

In a further experiment, the Canadian group (2006)[46] exposed several different cell lines (HL-60 and Mono Mac 6) to 1900 MHz pulsed RF fields at SAR levels of 1 and 10 W/kg at 37˚C—essentially the same protocol as used in their earlier 2006 study. Again, evaluation of levels of Hsp70 and Hsp27 expression showed no alterations in RF field-exposed cells of either type compared to analogous sham-exposed cells.

Vanderwaal et al. (2006)[47] exposed cultured HeLa, S3, and E.A. Hy296 cells to 847 MHz TDMA pulsed signal at SAR levels of 5 W/kg for 1, 2, or 24 hours, or to 900 MHz pulsed GSM signal at a SAR level of 3.7 W/kg for 1, 2, or 5 hours. Sham exposures were paired with each RF exposure, and a positive heat control arm (30 minutes at 45˚C or two hours at 41˚C) was also included. No increase in Hsp27 phosphorylation was seen in cells in either of the RF-exposed arms of the study by comparison with sham exposure. Both positive control arms saw an increase in Hsp27 phosphorylation, as expected.

French investigators, Sanchez et al. (2007),[48] exposed human skin cells (keratinocytes and fibroblasts) to 1800 MHz pulsed RF signal at an average SAR of 2 W/kg for 48 hours. A positive control (exposure to UVR in a single dose plus one hour at 45˚C) was

included in the protocol. Results showed no changes in Hsp70, Hsc70, or Hsp27 proteins in either keratinocytes or fibroblasts exposed to 1800 MHz RF fields for 24 hours compared to unexposed cells.

Chauhan et al. (2007)[49] in Canada, again exposed human glioblastoma cultured cells (U78MG) and a human monocyte cell line (MM6) to 1900 MHz pulsed RF signal at SARs of 0.1-10 W/kg intermittently (5 minutes on, 10 off) for a longer period (24 hours) instead of the six hours of the earlier studies. Gene expression was evaluated immediately after RF exposure and again 18 hours post-exposure, and no changes were seen in Hsp gene expression in the RF-exposed U78 MG or the MM6 cells. Positive control cells (43˚C for one hour) did show Hsp expression changes.

Franzellitti and his Italian colleagues (2008)[50] exposed human trophoblast cells to 1800 MHz continuous wave or pulsed GSM signal at a SAR of 2.0 W/kg for 4-24 hours intermittently (5 minutes on, 10 off) in a temperature controlled incubator and found Hsp70C transcript enhanced (but no protein) after 24 hours of pulsed signal compared to unexposed cells. Positive control cells (one hour at 43˚C) were also included in the experiment.

Valbonesi and colleagues (2008)[51] used HTR-8/SV neo cells exposed to pulsed 1817 MHz signal for one hour to determine whether Hsp70 or Hsc70 mediated stress response was elicited by comparison with control cells. No evidence was seen in RF-exposed cells for change in Hsp70 or Hsc70 gene or protein expression.

Table 6. Heat shock gene and protein expression changes and RF field exposure

Study	Cell Type	Exposure	Results	Comments
Czyz et al. (2004)[42]	P53 deficient and wild-type embryonic stem cells	1710 MHz pulsed RF Avg SAR 0.4-2.0 W/kg, 5 min on, 30 off for periods of 6-72 hrs	Up-regulation of Hsp70 in p53 deficient stem cells but not in wild type	
Miyakoshi et al. (2005)[18]	MO54 human glioma cells	1950 MHz IMT-2000 signal SAR 1-10 W/kg for 1-2 hrs	No change in expression of Hsp27 or Hsp70 proteins	
Wang et al. (2006)[43]	A 172 human glioblastoma cells	2450 MHz SAR 5-200 W/kg for 1-3 hrs or sham	No effect on Hsp70 or Hsp27 gene expression at 5 W/kg. Increase in phosphorylation of Hsp27 but only at 100 W/kg	Increase in protein phosphorylation may not be relevant due to high SAR levels

Study	Cell Type	Exposure	Results	Comments
Sanchez et al. (2006)[44]	Human cultured keratinocytes and human reconstructed epidermis (hRE)	900 MHz GSM; SAR 2 W/kg or sham for 48 hrs	No change in Hsp70, Hsp27 or Hsc70 in RF exposed keratinocytes. Increase in Hsp70 in hRE after 3-5 wks	Increase in Hsp 70 in hRE did not result in changes in thickness or proliferation
Chauhan et al. (2006a)[45]	Human lymphoblastoma cells	1900 MHz pulsed RF fields; SAR 1 or 10 W/kg or sham 5 min on, 10 min off for 6 hrs	No evidence of increased expression of Hsp70 or Hsp27 in RF-exposed cells compared to sham	Positive controls did show increased expression as expected
Chauhan et al. (2006b)[46]	HL-60 and Mono Mac 6 human derived cells	1900 MHz pulsed RF fields; SAR 1 or 10 W/kg or sham 5 min on, 10 min off for 6 hrs	No evidence of increased expression of Hsp70 or Hsp27 in RF-exposed cells compared to sham	
Vanderwaal et al. (2006)[47]	HeLa, S3 and EA Hy 296 cells	847 MHz TDMA signal; SAR 5 W/Kg or sham for 1, 2, or 24 hrs or 900 MHz pulsed GSM; SAR 3.7 W/kg for 1, 2, or 5 hrs	No increase in Hsp27 phosphorylation with exposure to either RF exposure for any cell line	Positive control (heat) showed increased phosphorylation in cell lines
Sanchez et al. (2007)[48]	Human keratinocytes and fibroblasts	1800 MHz pulsed signal; SAR 2 W/kg or sham continuous for 48 hrs	No effect of 48- hr RF fields on Hsp70, Hsc70 or Hsp27	Heat shock positive control; single dose of UVR + 45°C for 1 hr
Chauhan et al. (2007)[49]	U87MG human glioblastoma cells and monocytes	1900 MHz pulsed signal; SAR 0.1-10 W/kg; 5 min on and 10 min off for 6 or 24 hrs	No alterations in Hsp gene expression after 24 hrs exposure to RF fields	Positive heat shock control included
Franzellitti et al. (2008)[50]	Human trophoblasts	1800 MHz GSM continuous wave or pulsed signal; SAR 2 W/kg 5 min on, 30 off for 4-24 hrs or sham	Increased Hsp70C transcript in pulsed RF- exposed cells	Heat shock control cells (1 hr at 43°C used as positive control)
Valbonesi et al. (2008)[51]	HTR-8/SV neo human trophoblasts	1817 MHz pulsed signal; SAR 2 W/kg or sham for 1 hr	No evidence that exposure to RF induced Hsp70 stress response	

6A.5.2 Other gene and protein expression changes and RF fields (Table 7)

US investigators, Whitehead et al. (2006)[52] exposed cultured mouse C3H 10T 1/2 cells to 835 MHz Frequency Division Multiple Access (FDMA) or 847 MHz Code Division Multiple Access (CDMA) RF fields at a SAR of 5 W/kg or sham for 24 hours, using an Affymetrix U74AV2 gene chip (which employs 12,448 probes over 9198 genes) to search for oncogenes (genes involved in initiating cancer) or stress genes which were over or under expressed. Three separate flasks of cells were exposed to each of the two radiofrequencies, along with matched sham flasks. A positive control group of cells exposed to 0.68 Gy of x-rays included in the protocol demonstrated the expected gene expression changes by comparison with sham-exposed cells. However, the expression changes found in RF field-exposed cells versus the sham-exposed cells did not exceed the number seen in multiple comparisons of sham versus sham-exposed cells. The authors considered that the changes seen in RF exposed cells were false positives and concluded that there was no evidence that either 835 MHz FDMA or 847 MHz CDMA RF exposure altered gene expression.

Capri et al. (2006)[53] analysed levels of CD95 (a molecule which is important in starting and terminating the immunologic response) in CD4+ and in CD8+ T-cells in vitro in peripheral blood mononuclear cells taken from young (age 26 ± 5 years) and older (age 88 ± 2 years) donors and exposed or sham-exposed to 1800 MHz pulsed RF fields (SAR 2 W/kg) intermittently with or without stimulation by mitogens. Mitogens are agents which stimulate cell division. After RF exposure, a small but significant down-regulation of CD95 expression in mitogen-stimulated CD4+ T-lymphocytes was seen among older, but not younger donors. The fact that the down-regulation was seen only in older volunteers suggests that the RF-related effect, if real and eventually replicated in other studies, affects the relatively weaker immune systems seen in older individuals rather than the more robust systems seen in the young.

Tuschl et al. (2006)[54] evaluated human monocytes from donors for effects of exposure to 1950 MHz GSM basic signal or sham for eight hours, alternating five minutes on and 10 minutes off at a SAR of 1 W/kg. The study evaluated intracellular production of IL-2 and activity of immune relevant genes. No significant changes were seen in expression of products of immune relevant genes in RF-exposed cells after eight hours by comparison with sham-exposed cells.

The Canadian group noted earlier, Chauhan et al.,[46] exposed several different cell lines (HL-60 and Mono Mac 6) to 1900 MHz pulsed RF fields at SAR levels of 1 and 10 W/kg or sham at 37ºC to assess heat shock protein related genes. However, the investigators took advantage of the opportunity to measure changes in a number of proto-oncogenes (c-jun, c-myc, and c-fos) as well. Proto-oncogenes are normal genes which, through mutation or increased expression, can become oncogenes and initiate the process of carcinogenesis. No significant changes were seen in the expression of c-jun, c-myc or c-fos in either type of cells exposed to the pulsed RF fields by comparison

with sham-exposed cells. The findings mimic those noted in an earlier study by Czyz et al.[42] described in the section on heat shock gene and protein expression. In that study of p53 gene deficient and wild type embryonic stem cells exposed to 1710 MHz pulsed RF signal, exposure produced no change in levels of c-jun, or c-myc in wild type cells and only very modest and transient changes in the p53 deficient cells.

Zhao et al. (2007)[55] evaluated gene expression profiles in rat neurons exposed to 1800 MHz pulsed GSM signal 10 minutes on and 5 minutes off for 24 hours at an average SAR of 2.0 W/kg or sham in a test chamber at 37°C. Among 1,200 candidate genes evaluated using an Affymetrix U34 gene chip, 24 were up-regulated and an additional 10 were down-regulated after 24-hour intermittent exposure at an average SAR of 2.0 W/kg. The genes were associated with multiple cellular functions including signal transduction pathway and metabolism. Some caution is needed in interpreting these results because, although statistically significant p-values were found for the 34 genes, none of the up-regulated change values exceeded two-fold, and many are as little as 1.15, suggesting the possibility of false positive findings due to chance in so many markers.

Zhadobov and colleagues in France (2007)[56] exposed U25 human glioma cultured cells to 60 GHz low power fields at power densities of 0.5 m W/cm^2 or 5.4 $\mu W/cm^2$ for periods of 1 to 33 hours in an incubator to achieve adequate temperature control. The 60 GHz range has a number of upcoming applications including use in indoor high-data rate communications over wireless 4G local area networks (LAN). No changes in expression of any stress-sensitive genes were seen compared to sham-exposed cells.

Gerner et al. (2010)[57] exposed human Jurkat cells, human diploid fibroblasts, and quiescent mononuclear cells to 1800 MHz pulsed signal at a SAR of 2 W/kg or sham for eight hours and found increases in protein synthesis in both Jurkat cells and fibroblasts exposed to RF fields, by comparison with sham-exposed cells, but no difference in the exposed quiescent mononuclear cells. The authors interpreted the results as indicating an increased protein in the cells turnover due to interference in hydrogen bonds by RF fields.

Japanese scientists, Hirose et al. (2010),[58] studied the effect of 1950 MHz modulated IMT-2000 W-CDMA signal at SARs of 0.2, 0.8 and 2.0 W/kg or sham exposure for two hours on rat microglial cells. Results were assessed at 24 and 72 hours after exposure, and no significant differences were seen between RF-exposed cells and sham-exposed cells for expression of immune related cytokines including tumour necrosis factor-α, interleukin 1-β, or IL6. Cytokines are regulatory proteins that play a central role in the immune system by modulating functions in the system, including lymphocyte activation, immune cell proliferation, differentiation, and survival.

Table 7. Other gene and protein expression changes and RF exposure

Study	Cell Type	Exposure	Results	Comments
Whitehead et al. (2006)[52]	Cultured mouse fibroblasts	835 or 847 MHz FDMA or CDMA signal; SAR 5 W/kg or sham for 24 hrs	No difference in number of gene expression changes in RF exposed cells vs. sham than the number seen in sham vs. sham comparisons	Authors concluded that neither RF frequency altered gene expression
Capri et al. (2006)[53]	Human lymphocytes	1800 MHz pulsed signal; SAR 2 W/kg or sham; 10 min on 20, off for 44 hrs with or without mitogen stimulus	Down regulation of CD95 expression in stimulated CD4+ T-lymphocytes from older but not younger donors	
Tuschl et al. (2006)[54]	Human monocytes	1950 MHz GSM basic signal; SAR 1 W/kg; 5 min on, 10 off for 8 hrs	No significant changes in immune- related gene products including IL-2, INF, and TNFα	
Chauhan et al. (2006b)[46]	HL-60 and Mono Mac 6 human-derived cells	1900 MHz pulsed RF fields; SAR 1 or 10 W/kg or sham 5 min on, 10 min off for 6 hrs	No increase in expression of the proto-oncogenes c-jun, c-myc, and c-fos	
Zhao et al. (2007a)[55]	Rat neurons	1800 MHz pulsed GSM signal; SAR 2.0 W/kg, or sham 10 min on 5 off for 24 hrs	24 genes up-regulated and 10 down- regulated after RF exposure, compared to sham	
Zhadobov et al. (2007)[56]	U251 human glioma cells	60 GHz RF low power signal; power density 0.5 mW/cm² or 5.4 μW/cm² or sham for 1–33 hrs	No modification of stress- sensitive gene expression	Carried out in incubator for temperature control

Study	Cell Type	Exposure	Results	Comments
Gerner et al. (2010)[57]	Human Jurkat cells; human diploidfibroblasts; human quiescent mononuclear cells	1800 MHz pulsed GSM signal; SAR 2.0 W/kg or sham for 8 hrs	Increased protein synthesis in Jurkat cells and human fibroblasts in RF-exposed vs. sham-exposed cells	No change due to RF exposure in quiescent mononuclear cells
Hirose et al. (2010)[58]	Rat microglial cells	1950 MHz modulated IMT-2000 W-CDMA signal; SAR 0.2, 0.8, 2.0 W/kg or sham for 2 hrs	No differences between RF- and sham- exposed cells in cell activation or expression of immune function cytokines	

Summary

Overall, although some recent studies have shown alterations in heat shock-related gene expression or protein expression, a similar number or more have shown negative results. The same situation prevails in studies of RF fields and other non-heat shock-related gene and protein expression studies. As in other areas of investigation concerning potentially adverse effects of RF fields on physiological processes in cell cultures, most recent studies are well-conducted, and there are no specific features which appear to distinguish positive studies from those finding no association. Although this area of research will undoubtedly continue, there is no compelling evidence at present that RF fields of the type and strength to which humans are exposed are responsible for gene or protein expression changes.

6A.6 Other Specific Intracellular Effects

6A.6.1 Changes in protein and RF fields (Table 8)

In addition to gene expression changes, which could result in over- or under-production of proteins, other studies have been conducted to determine whether exposure to RF fields can alter physiologic processes within different types of cells.

Belyaev et al. (2005)[59] conducted a study to evaluate whether there were differences in response to RF fields in lymphocytes taken from electro-sensitive individuals by comparison with those from non-sensitive subjects. The research group exposed human lymphocytes from seven healthy individuals and seven electro-sensitive persons to 915 MHz GSM signal at SAR of 37 mW/kg or sham for a period of two hours, in a TEM cell. The study was conducted to determine whether RF exposure altered chromatin conformation in electro-sensitive individuals by comparison with non-

sensitive subjects. Chromatin conformation capture examines protein-DNA combination in chromosome structures within the cell nucleus which have a variety of functions including helping facilitate gene expression. A positive control group was also part of the protocol and cells in this group were exposed to 41°C for two hours. Evaluation at 24 and 48 hours after exposure showed changes in the conformation of chromatin in lymphocytes from both radio-sensitive and non-sensitive RF-exposed subjects compared with sham-exposed cells from each group. No significant differences were seen between healthy and electrically sensitive participants. The authors reported that the changes seen in the RF-exposed cells were similar to the stress response seen in the positive control heat shock cells.

A German study, Sukhotina et al. (2006)[60] attempted to confirm results of an earlier investigation[61] conducted back in 2002 suggesting that melatonin synthesis is suppressed by exposure to RF fields. Isolated hamster pineal glands were exposed to 1800 MHz continuous wave or pulsed GSM signal at SAR levels of 8, 80, 800, and 2700 mW/kg for periods of seven hours, and perfusate samples were collected every hour. At SAR rates characteristic of the use of mobile phones (8, 80, and 800 mW/kg) melatonin release was enhanced by both continuous and pulsed exposure by comparison with control glands. At 2.7 W/kg pulsed 1800 MHz exposure appeared to suppress melatonin levels, but as the exposure increased temperature by 1.2°C, the suppression was actually due to thermal effects. The authors concluded that the study did not support the theory that exposure to RF fields at levels produced by use of mobile phones suppresses melatonin.

Friedman et al. (2007)[62] studied the effect of RF fields on mitogen activated protein kinase (MAPK) cascades, which are important in cell survival and apoptosis. The investigators subjected human cultured epithelial (HeLa) cells and Rat 1 cells to 875 MHz at intensities of 0.005–0.3 mW/cm^2 for periods of 0, 5, 10, 20, or 30 minutes. Results showed a temporary increase in phosphorylation of extracellular signal-regulated kinase (ERK), one of the MAPK pathways, at five minutes, which decreased to basal levels within 30 minutes. The authors suggested that the activation of ERK is mediated by reactive oxygen species (ROS) produced by the RF fields, and the ERK activates the MAPK cascade in both types of cells tested. The authors suggest the finding might indicate that interference with intracellular signalling by RF fields can inappropriately activate ERK functioning with adverse effects on apoptosis. However, it should be noted that studies of RF fields and apoptosis have been predominantly negative.

Bormusov et al. (2008)[63] in Israel evaluated the possibility that RF field exposure might damage eye tissue. The investigators exposed bovine lenses to 1100 MHz RF fields at 2.22 mW intensity for 90 cycles of 50 minutes each, followed by a 10-minute pause. The lenses were then cultured for 15 days. Control lenses were simply cultured for 10–15 days. A further group was exposed to heat (39.5°C) three times for two hours each time with 24 hours between exposures and cultured for 11 days. Results showed

reversible decreases in lens optical quality as well as irreversible biochemical and morphological damage to the epithelial layer of the lens in the group exposed to RF fields compared with the control group. The authors reported that the damage to the lens in the RF-exposed group was distinctly different from that seen as a result of heat. No studies have yet confirmed these findings.

Cespedes and Ueno (2009)[64] evaluated whether the magnetic component of the fields that RF exposure generates might have an effect on ferritin, an iron-cage protein that stores iron for release over time, as required in normal cellular physiology. Ferritin was isolated from equine spleen cells and exposed to a 1 MHz RF field with a magnetic component of 30 μT for up to nine hours. Iron release was measured over this time period. The maximum release occurred by about five hours of exposure. Abnormal release might affect the ability of ferritin to uptake and store iron; however, the authors note that the effects seen in the study would not occur in a healthy individual with normal iron levels but might have relevance for those with hemochromatosis, a genetic disease characterized by high levels of iron in the blood.

Table 8. Protein changes and RF fields

Study	Cell Type	Exposure	Results	Comments
Belyaev et al. (2005)[59]	Lymphocytes taken from electro-sensitive vs. non-sensitive subjects	915 MHz GSM pulsed signal; SAR 37 mW/kg or sham for 2 hrs	Alterations in chromatin conformation in RF-exposed cells from both electro-sensitive and non-sensitive individuals	No significant differences between RF- exposed lymphocytes from electro-sensitive vs. non-sensitive individuals
Sukhotina et al. (2006)[60]	Hamster pineal gland	1800 MHZ CW or pulsed GSM signal; SAR 8, 80, 800, 2700 mW/kg for 7 hrs	Melatonin synthesis increased with CW and pulsed RF at 800 mW/kg and suppressed by pulsed signal 2700 mW/kg	Suppression by pulsed signal at 2700 mW/kg due to thermal effects (+1.2°C heating)
Friedman et al. (2007)[62]	HeLa cells and Rat 1 cells	875 MHz at intensity of 0.005–0.3 mW/cm^2 for 5, 10, 20, or 30 min or sham	Activation of MAPK cascades in RF-exposed cells	No SAR presented
Bormusov et al. (2008)[63]	Bovine organ cultured lens tissue	1100 MHz at 2.22 mW intensity for 192 cycles of 50 min with 10-min pauses or control	Adverse effects on lens quality due to enhanced enzyme activity in RF-exposed lenses	No SAR presented
Cespedes and Ueno (2009)[64]	Ferritin, an iron holding protein	1.0 MHz exposure with a magnetic field of 30 μT for 0–9 hrs	Abnormal iron release by ferritin protein	

Summary

It is difficult to draw conclusions from the evidence from studies in this area at present. Although all of these representative studies indicate that RF fields may affect physiologic processes, the studies have a variety of endpoints, and essentially none of the different findings have been independently replicated. As well, none provide the basis for a convincing biologic mechanism for the action of RF fields. If replicated, the in vitro changes seen in culture would need to be tested in animal models to see whether they persist in the face of interactions that take place in living organisms.

The most frequently used cells for examining the effect of RF fields on single cell motility are sperm cells as their characteristics are well-known, and they are easy to obtain. A complete review of issues surrounding the effects of RF fields and male fertility, including analysis of sperm cells is presented in Section 10.

6A.6.2 Calcium efflux and RF fields (Table 9)

Cells control internal calcium levels tightly, and it is known that a number of cell-signalling pathways include temporary changes in intracellular calcium. Early studies had indicated that pulsed RF fields might allow calcium efflux from brain tissue,[65-67] although the evidence appearing in more recent studies is quite contradictory. Since 2006, only three new studies have appeared.

Platano et al. (2007)[67] exposed neurons from Sprague-Dawley rats to one, two, or three sessions of 90-second exposure to 900 MHz continuous wave or pulsed RF fields at SAR 2 W/kg for each type of RF exposure to evaluate whether voltage-gated calcium channels (VGCC) were affected in their ability to control calcium levels in cells. VGCCs are an important transport system for moving sodium and calcium ions in and out of cells. In conducting the experiment, the investigators used Ba^{2+} ions in order to avoid Ca^{2+} inactivation of the currents induced with RF fields. Results showed no alterations in voltage-gates calcium channel brought about by either the continuous wave or pulsed 900 MHz exposure.

Rao et al. (2008)[68] in the US, exposed neuronal cells from a mouse embryonic cell line to 700 –1100 MHz signal at 100 MHz intervals at 0.5 to 5 W/kg for one hour. The study found that at 800 MHz (SAR .5 W/kg), the number of Ca^{2+} spikes per hour was significantly greater than the number on the control cells. The authors reported that the increase was RF frequency dependent but not SAR dependent.

A recent study, O'Connor et al. (2010)[69] exposed human endothelial cells, PC-12, neuroblastoma cells and primary hippocampal neurons to a pulsed 900 MHz GSM signal at SAR levels from .012–2 W/kg, similar to the levels incurred using a GSM mobile phone, for a period of 30 minutes. Data from the pulsed field experiment were compared to analogous result using a continuous wave signal or sham. Neither the pulsed nor the continuous wave exposure had any effect on Ca^{2+} signalling even at the

highest SAR levels. The evidence for any effect of RF fields on calcium channelling remains uncertain.

Table 9. Calcium efflux and RF fields

Study	Cell Type	Exposure	Result	Comments
Platano et al. (2007)[67]	Sprague-Dawley rat-cultured neurons	900 MHz pulsed or continuous wave exposure for 1, 2 , or 3 sessions of 90 sec	No changes seen in voltage-gated calcium channels from pulsed or CW exposure	
Rao et al. (2008)[68]	Mouse embryonic neurons	700–1100 MHz signal; SAR .5–5 W/kg for 60 min + control cells	Cells exposed to 800 MHz fields had significantly more Ca^{2+} spikes per hour than control cells	
O'Connor et al. (2010)[69]	Human endothelial cells, PC-12 neuroblastoma cells, and primary hippocampal neurons	900 MHz GSm pulsed or CW signal; SAR .12–2 W/kg or sham for 30 min	No change in Ca^{2+} signaling in any cell type with pulsed or CW exposure compared to sham exposed	

Summary

There is little evidence from recent studies that RF fields adversely affect calcium channelling in cell cultures.

6A.6.3 Cell permeability and RF fields (Table 10)

Although most work on possible effects of RF fields on blood-brain barrier permeability are carried out in animal models (reviewed in Section 6B), there have been several studies since 2005 looking at permeability after RF exposure in endothelial cells.

Franke et al. (2005)[70] exposed an endothelial cell/astrocyte co-culture model to pulsed 1800 MHz RF fields at SARs of 0.03 or 0.46 W/kg or sham over five days in an attempt to confirm findings from an earlier study[71] conducted in 2000 which showed increased permeability with RF exposure. The co-culture cell model used in the present paper featured significantly higher physiologic tightness than that used in the 2000 study and more closely mimicked blood-brain barrier characteristics in living animals. Results showed that the outcome measure, sucrose permeation across the cell layers, was not affected by exposure to the 1800 MHz RF exposure.

A further study by the same group[72] used brain capillary endothelial cells isolated from pigs and cultured on a collagen-coated Transwell cell culture insert to mimic the blood-brain barrier to test for disruption by RF fields. The cultured multi-cell membranes were exposed to 1966 MHz UMTS signal or sham exposure for between 24 and 72

hours in a temperature-controlled incubator at a maximum SAR of 1.8 W/kg. No adverse effects from RF exposure were seen on barrier tightness, transport behaviour, or integrity of tight-junction proteins.

Kuo and Kuo (2008)[73] in Taiwan designed an experimental system, the aim of which was to increase permeability of the blood-brain barrier to anti-HIV drugs. They cultured human brain microvascular endothelial cells on a polycarbonate membrane coated with human fibronectin and rat-tail collagen to mimic the barrier in vitro, exposed the barrier to 915 MHz for 90 minutes, and found the RF exposure increased the permeability of the barrier to Saquinavir, an anti-HIV agent.

Table 10. Blood-brain barrier permeability and RF fields

Study	Cell Type	Exposure	Results	Comments
Franke et al. (2005a)[72]	Co-culture of rat astrocytes and endothelial cells	1800 MHz pulsed GSM signal; SAR 0.3 W/kg for 1–5 days	No sucrose permeation across cell layers unaffected by RF field exposure	Results did not replicate group's previous positive study
Franke et al. (2005b)[70]	Cultured pig brain capillary endothelial cells	1966 MHz UMTS signal; SAR 1.8 W/kg or sham for 24–72 hrs	No evidence of RF effect on function of BBB	
Kuo and Kuo (2008)[73]	Cultured human brain microvascular endothelial cells	915 MHz continuous wave at 5 mW for 90 min	Increased permeability to Saquinavir, an anti-HIV agent	

Summary

The relatively small number of recent studies suggests that cell system models in vitro for assessing blood-brain barrier permeability are being superseded by more investigations in animals.

6A.5 Discussion

There have been many in vitro studies over the past six or seven years looking at possible mechanisms by which RF fields might adversely affect cell systems and, by extension, human health. However, the results of investigations in each topic area still tend to be divergent and contradictory. Studies done to try to replicate positive results most often turn out negative, without clear methodologically-based reasons why results diverge.

There is no consistent evidence that RF fields produce chromosomal aberrations or micronucleus formation or that they generate the type of DNA damage characteristic of carcinogenic mechanisms. Recent evidence does not appear to support the notion that RF fields cause mutations or cell transformation. Studies of the effect of RF fields on cell proliferation have, in the main, been negative although in some cases results have indicated reduced cell proliferation. Studies looking at the production of ROS have been contradictory, and this field will require still more research. Early evidence that RF fields might stimulate ODC activity has not been confirmed by results from recent studies. Several apoptosis studies have shown positive results, but an equal or greater number have shown no effect. In vitro studies designed to explore whether RF fields facilitate leakage through the blood-brain barrier have not shown any consistent evidence of any effect due to RF fields. Most research on blood-brain barrier permeability is currently is being carried out in animal models.

Finally, there is no agreement as to which types of cells might be most sensitive to adverse effects of RF fields and no agreement on which RF frequencies and characteristics are most likely to elicit a biological effect. Because of this, no plausible mechanism has emerged to explain how RF fields might produce adverse biologic effects.

At the present time, there is no convincing body of evidence from in vitro investigations that exposure to RF fields at levels expected in day-to-day use of mobile phones and other RF emitting devices have the ability to initiate adverse biologic processes characteristic of human disease.

6A.5.1 Research gaps

More research is needed to:

- Encourage some degree of standardization among research protocols investigating any given putative adverse effect to allow direct comparisons with other studies to confirm or refute positive findings.
- Explore the joint effects of RF fields in conjunction with known cellular-stressing agents.
- Evaluate cellular response to RF in cells obtained from younger versus older donors.
- Develop cellular models that are more closely related to human biological processes.

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Section 6

Biological Effects of Radiofrequency Field Exposure

Section 6B Animal Studies

Table of Contents

Summary

- Studies using animals have historically proven useful for investigating health effects; a large number of such studies have recently been conducted (2005–2012) to evaluate whether exposure to radiofrequency (RF) fields has adverse biological effects.
- Long-term bioassays, designed to determine whether RF exposure either alone or in conjunction with known mutagens can initiate or promote development of cancer in animals, have been uniformly negative.
- Studies of RF fields and toxicological effects such as DNA damage, micronucleus formation, apoptosis, reactive oxygen species, and gene expression changes have been inconsistent and the results contradictory. Positive studies have proven difficult to replicate. This lack of consistency reduces the likelihood that exposure to RF fields has toxicological effects in animals.
- There is no consistent evidence that exposure to RF fields produces biological effects in animal central nervous systems. Most recent investigations have been unable to confirm Swedish studies suggesting that RF exposure alters blood-brain barrier permeability; however, other aspects of brain physiology are less well studied. Behavioural investigations of the role of RF exposure on animal learning and cognitive function are mixed, with most being negative.
- Immune function studies have been mostly negative, although most of the studies to date have been conducted in adult animals. Earlier Soviet study results, indicating that serum taken from RF-exposed animals could increase embryo mortality when injected intraperitoneally into pregnant rats, have not been confirmed. Notwithstanding this, more studies are needed on RF effects in young animals.
- Effects of RF exposure on endocrine function, particularly on melatonin levels, have been negative, and studies of their effect on reproductive function in female animals have also been negative.
- Overall, studies have not shown convincing evidence that RF field exposure produces adverse biologic effects in animals. There are many negative results, and the relatively few positive results are rarely replicated in confirmatory studies. Most of the recent studies are characterized by good research protocols including appropriate control of thermal effects and excellent animal care along with appropriate use of reverberation chambers to ensure uniform specific absorption rates (SAR) in whole body RF dosimetry, or of animal restraints in the case of RF fields applied to specific organs such as the brain. These recent studies have generally shown no association of specific outcomes with exposure to RF.
- There is no recognized biologic mechanism by which RF exposure might operate to cause adverse biological effects in animals.

6B.1 Introduction

The use of animal models is common in testing for potential adverse (or beneficial) effects of exposure to a variety of agents in the environment. These agents include forms of non-ionizing radiation such as ultraviolet (UV) light and RF fields. Animals carry many genes analogous to those in humans, and have similarities in embryogenesis, development, and other physiological processes which could help predict possible biological effects in man. Unlike experiments carried out in isolated cell cultures, use of animal models allows for study of the physiological interactions which take place in living systems.

Research using animals is conducted using several animal types; the most common being rats and mice. While different anatomically and physiologically from humans, and with a much shorter lifespan, other aspects of their physiology, such as their DNA repair mechanisms, are very similar to those in humans. Barring differences resulting from species-specific sensitivity to the effects of a particular exposure, animal testing can reveal biologic effects which are very relevant to humans.

The nature of the putative effect to be studied sometimes dictates which type of animal is selected for a study. Long-term bioassays—used to study carcinogenesis and discussed below—normally use outbred or hybrid strains of rodents, as their genetic diversity closely mimics human diversity. Some studies are carried out in animal models that demonstrate a predisposition to a disease as a result of genetic alterations or exposure to a specific chemical or physical agent that initiates or accelerates the disease process. Use of animals for studies must also take into consideration the nature of the effects a particular agent may have on the animal over and above the effect being tested. One of the issues of significant importance to the study of the effects of RF fields is that, like all microwaves, the fields may have a local heating effect, particularly in small animals. Increased core heating by as little as 1˚C is known to affect several aspects of physiology.[1] Humans are much bigger than lab animals, and consequently any potential local heating effect might be diffused more quickly, and be less likely to affect physiology. Further, the power levels of RF devices in common use and of most human concern such as mobile phones generate specific absorption rates (SAR) within the human body which are too low to generate any thermal effects. Animal testing which focuses on the non-thermal effects from energy deposition due to day-to-day use of RF-emitting devices may be of relevance to human disease.

In order to avoid potential localized heating generated by RF fields, investigators in recent animal studies have evolved specialized laboratory devices such as rotating carousels and anechoic or reverberation chambers to improve control and uniformity of RF dosimetry in small animals. Examples of this include a rotating “ferris wheel” exposure instrument mechanism[2] or the carousel proposed as by Kuster and colleagues (2006).[3] Such devices have given more recent studies better control over thermal effects, and equally importantly, more precision in the actual RF dose

administered. Specialized exposure vessels such as anechoic and reverberation chambers, allow animals freedom of movement and hence allow exposure to low levels of RF fields for much longer periods of time—much like those seen in human activity. However, animal exposures in such chambers are "whole body" and cannot be restricted to specific organs such as the brain alone. For more precise measurement of exposure devices such as polycarbonate "capsules" are used in which small animals are placed to restrain them in position in order to help attain precise SAR in small organs such as the brain. These devices have been found to reduce animal distress during exposure, which is valuable from a humane perspective, but also act to reduce stress-related physiologic effects which might confound study results. However, use of restraints also restricts the amount of time that animals can be exposed to RF fields.

While use of the technologic advances such as those described above is more common in recent studies, some investigations used crude techniques such as a mobile phone placed in the cage as a RF field source. The resulting exposure to individual animals, and especially to specific organs, is ill-defined and cannot meet current RF dosimetry standards essential to proper interpretation of experimental results.[3]

6B.2 Purpose

The objective of the section is to summarize the state of knowledge from animal studies concerning possible adverse health effects of RF fields. The intent is to focus specifically on research conducted from around 2005–2006 in order to take advantage of the improved study protocols and RF exposure technology incorporated into recent studies.

6B.3 Methods

A search of the online databases PubMed (MEDLINE) and EBSCO Academic Search was conducted using search terms "radiofrequency field," "radiofrequency radiation," "RF radiation," "microwave," "cellular phone," and "mobile phone," and these terms were combined with terms for cancer, carcinogenesis, DNA damage, apoptosis, gene expression, reactive oxygen species, protein expression, blood-brain-barrier permeability, brain physiology, central nervous system effects, immune function, endocrine function, and female reproductive function. The search was restricted to peer-reviewed articles published in English, during the period 1990–2011, and then a filter was applied to identify studies conducted in animals, reducing these to 380 after elimination of duplicates. Restricting studies to those published since 2005 and eliminating duplicate references picked up in more than one search reduced the number to 142 for more detailed review. A separate search using the term "WiFi" linked to cancer, and various other terms including "health," produced only two animal investigations. Review articles were separated out so bibliographies could be searched; and recent national reviews of RF fields and health such as the Latin American Experts Committee on High Frequency Electromagnetic Fields and Human Health report (2010)[4]

and the UK Health Protection Agency's recent report (2012)[5] were also examined for papers missed by other means.

This review concentrates mainly on more recent studies (2005–2011), although summary paragraphs at the end of each group of potential adverse biological effects will consider all available evidence and not just studies conducted since 2005. The reason for the emphasis on more recent work is that these investigations are more likely to be characterized by good RF dosimetry and better control of the potential confounding effects of thermal changes due to RF exposure. Sometimes, investigations conducted many years ago will be referenced to provide context for study of a particular possible adverse effect. For example, several studies conducted in the Soviet Union in the 1980s are referenced as their reported biologic effects provided the impetus for recent (2009–2010) investigations. Tabular data will similarly emphasize recent studies rather than older ones published prior to 2005. Due to their high cost and long duration, animal carcinogenesis bioassays are relatively uncommon, so key studies back to 1992 will be considered.

Major categories of potential adverse biologic effects (cancer, neurologic function, immune effects, etc.) will be discussed. Within each category, a representative group of studies has been chosen for tabular presentation and discussion. These studies are, for the most part, characterized by good descriptions of RF dosimetry, use of RF frequencies that humans are exposed to on a day-to-day basis (such as Global System for Mobile Communication [GSM] and Code Division Multiple Access [CDMA] mobile phone frequencies), appropriate use of animal restraints and exposure system technology to ensure accurate organ-specific or whole body SAR values, and maximum SAR values of around 2 W/kg. On occasion, findings which may not satisfy these selection criteria but have been influential in public or scientific discussions of RF and health are also included.

6B.4 Cancer and RF Exposure

Perhaps the single greatest long-term public concern with use of RF wireless technology is whether it has the ability to initiate or promote the development of cancer. In general, carcinogenesis studies are grouped into the following categories:

1. Long-term two-year bioassays performed to detect increased incidence of spontaneous malignancies in outbred animals

2. Studies on tumour-prone animals designed to determine whether RF exposure alone increases the incidence of specific cancers

3. Studies to determine whether RF exposure increases the incidence of specific cancers initiated by known carcinogens such as dimethylbenz(a)anthracene (DMBA) or prenatal N-ethyl-N-nitrosourea (EMU).

A number of high quality studies have been conducted on each of these topics.

The first group, long-term bioassays, are studies of up to two years in duration, which are conducted in mice or rats. The studies follow very well defined criteria, with animals exposed to a test agent for relatively long periods of time. Animal group sizes are large and study designs usually include histopathologic evaluation (a microscopic examination to detect abnormalities at the cellular level) of samples of forty or more different tissues per animal. Exposure to the chemical or agent of interest commonly begins when animals are young and continues for up to two years. Bioassays (and most animal studies) include a so-called sham group which serves as a control group. These animals are exposed to all the same conditions that the other experimental animals except for the RF field. This helps to ensure that any adverse effects seen in the exposed animals are due to the RF exposure itself and not to other factors such as diet, confinement, stress, etc.

Independent analyses by the International Agency for Research on Cancer and the U.S. National Toxicology Program have shown in general that results of the two-year bioassays in rodents have a high predictive value for cancer in humans. These studies are commonly accepted by regulatory agencies as providing the most complete assessment of carcinogenicity,[6] the process by which normal cells become cancerous.

6B.4.1 Cancer and RF exposure – long- term bioassays (Table 1)

Chou and colleagues (1992)[7] exposed 200 Sprague-Dawley rats to 2450 MHz pulsed signal at SARs of 0.4 W/kg for a 200 gram animal to 0.15 W/kg for an animal weighing 800 grams, or sham for 21.5 hours per day, 7 days per week for a period of 25 months in order to determine whether two years of exposure altered the incidence of cancer in the animals compared to controls. The exposure began at eight weeks of life. All animals were histopathologically examined as they died during the course of the study, and at 25 months all surviving rats were euthanized and had a complete examination. No significant differences were seen between RF-exposed animals and the control rats for tumour incidence at any site.

A further study by La Regina et al. (2003)[8] involved exposing 80 male and 80 female Fischer rats to either 835 MHz FDMA or 847 MHz CDMA modulated RF fields for four hours a day, five days per week for two years in individual restraining devices within insulated exposure chambers. The authors reported that by the end of the first few days of the study, rats became familiar with the restraint process and most were sleeping at the end of each RF exposure. No indications of stress were reported by the investigators. Time-averaged SAR in the brain tissue of the exposed rats was about 0.85 W/kg. A third group of 80 male and 80 female rats underwent sham exposure under the same conditions. At the end of the study, surviving rats were killed and necropsied, and all data on these rats and those dying during the course of the study were analysed. The number and type of tumours were compared for each of the RF-exposed groups to that seen in the sham rats. No significant differences in malignant or benign tumours at any anatomic site were seen between RF-exposed and sham-

exposed rats. No significant differences were seen between groups in body weight or overall health.

Anderson et al. (2004)[9] obtained three sets of 36 pregnant Fischer 344 rats and exposed them to a 1600 MHz signal at 19 days of gestation for two hours per day, five days per week. Exposure of their 700 pups continued to 23 days after parturition. From these pups, 90 males and 90 females were assigned to each of three groups. One was exposed at 1.6 W/kg a second at 0.16 W/kg, and the third group became sham controls. An additional 80 male and 80 female pups served as cage controls—animals which are not exposed to either the RF fields or to the physical conditions of the exposed and sham-exposed animals. Near field RF of two hours per day, five days per week was continued in the exposed groups until the rats were two years old. At the end of the study, no significant differences were seen in cancers between the RF-exposed and sham-exposed rats. Percentages of male animals surviving to the end of the study did not vary by exposure group, although among females a decrease in survival time was seen in the cage control group who were not exposed to RF. The results for this study are similar to those seen in several other long-term Fischer 344 rat investigations designed to determine whether RF exposure promotes tumours initiated by administration of ENU prenatally.[10,11]

Smith and colleagues (2007)[12] exposed 65 male and 65 female Wistar rats to 902 MHz GSM or 1747 MHz Digital-Coded Squelch (DCS) signal at three nominal SAR values: 0.44, or 1.33, or 4.0 W/kg. Exposure was carried out for two hours per day, five days per week for 52 consecutive weeks (30 rats per group) or for 104 weeks (100 rats per group). During exposure the rats were confined in polycarbonate tubes within an electromagnetically isolated carousel. A sham-exposed and a cage control group were included in the study. At the end of the studies (52 weeks and 104 weeks exposure), rats which had survived were euthanized, and tissue from all rats was examined microscopically. No significant differences were seen between the RF-exposed and sham-exposed rats in body weight, mean individual organ weights, or numbers or types of non-neoplastic or neoplastic tumours.

Tillman and colleagues (2007)[13] designed a study to evaluate possible carcinogenic effects from RF field exposure in B6C3F1 mice. The mice were divided into groups of 65 and were exposed to 902 MHz GSM or 1747 MHz DCS signal at low (0.4 W/kg), medium (1.3 W/kg) or high (4.0 W/kg) SAR levels. Similar numbers of mice were assigned to either sham or to cage control status. Mice were exposed to RF fields or sham two hours per day, five days per week over a period of two years while restrained in tubes. Tubes were mounted in “ferris wheel” type exposure systems to equalize SAR to each rat within exposure categories. At the end of two years, surviving mice were euthanized. A uniform microscopic tissue examination was carried out on these mice and all mice dying in the course of the study. No differences in mortality during the course of the study or in tumour type or incidence rates were seen between RF-exposed and sham-exposed groups of mice.

A further study by Bartsch et al. (2010),[14] originally designed to study the effects of 902 MHz GSM long-term exposure on Sprague-Dawley rats, was unevaluable for cancer outcomes due to insufficient data and potentially inadequate pathologic examination of the animals.

All of the long-term bioassays evaluating spontaneous tumour development due to exposure to long courses of RF field exposure have been convincingly negative and were mostly carried out on 2G GSM-pulsed wireless systems.

Table 1. Cancer bioassays and RF field exposure in rat and mouse animal models

Study	Animal Species/ Strain	Exposure	Tumour	Results	Comments
Chou et al. (1992)[7]	200 Sprague-Dawley rats	2450 MHz pulsed signal; SAR 0.15–0.4 W/kg or sham for 21.5 hrs/day, 7 days/wk, for 25 mos	Spontaneous tumours	No significant difference in RF- exposed vs. control rats	Complete histopathology on all animals
LaRegina et al. (2003)[8]	480 Fischer 344 rats	835 MHZ FDMA or 847 MHz CDMA signal; SAR brain 0.85 W/kg or sham 4 hrs/day, 5 days/wk for 2 yrs	Spontaneous cancers	No significant difference in RF- exposed vs. control rats	Complete histopathology
Anderson et al. (2004)[9]	700 Fischer 344 rats	1600 MHz signal; SAR 0.16 or 1.6 W/kg or sham; 2 hrs/day, 7 days/wk for 2 yrs	Spontaneous cancers	No significant difference in RF- exposed vs. control rats	Complete histopathology
Smith et al. (2007)[12]	1170 Wistar rats	902 MHz GSM pulsed and handover; or 1747 MHz; SAR 0.4, 1.3 or 4.0 W/kg or sham 2hrs/day, 5 days/wk, for 1 or 2 yrs	Spontaneous tumours	No difference between 902 MHz or 1747 MHz RF-exposed vs. control rats	
Tillman et al. (2007)[13]	1170 B6C3F1 mice	902 MHz GSM and 1747 MHz DCS in basic and talk modes SAR levels of 0.4, 1.3, 4.0 W/kg; 2 hrs/day, 5 days/wk for 2 yrs	Liver tumours or their precursors	No effect of RF on hepato-cellular tumours	No health effects attributable to RF exposure

6B.4.2 Cancer in tumour- prone animals and RF exposure (Table 2)

Another group of cancer studies involves animals bred for susceptibility to a specific tumour. The study which galvanized interest in whether RF exposure might enhance cancer incidence in tumour-prone animals was conducted originally in 1997.[15] The investigators exposed Eμ-*pim*-1 transgenic mice (which develop lymphoma at a high rate) to 900 MHz GSM pulsed RF fields or sham twice per day for 30 minutes, seven days per week beginning at six to eight weeks of age and continuing up to 18 months at SAR values of between 0.13 and 1.4 W/kg. Mice were examined frequently during the course of the study for development of lymphoma. At the end of the study, those mice which had survived were discarded rather than being histopathologically examined—a weak point in the investigation as examination of all participating animals was therefore incomplete. A 2.4-fold increase in lymphoma was reported in the mice exposed to 900 MHz RF fields by comparison with sham animals.

Utteridge and colleagues (2002)[16] attempted to replicate the findings of the 1997 study. They exposed Eμ-*pim*-1 mice to a 898 MHz pulse modulated RF signal at SAR levels of 0.25, 1.0, 2.0, and 4.0 W/Kg one hour per day, five days per week for up to 104 weeks. Sham and cage control groups were also included in the study. Mice were restrained in plastic tubes during RF exposure, which took place on a carousel device designed to ensure uniform RF exposure to all mice in each group. Complete pathologic examination was carried out on all mice either at death during the study or at study termination. No significant differences in lymphoma incidence were seen between RF-exposed mice at any SAR level and sham-exposed animals.

A further attempt to replicate the findings of the 1997 study was conducted by Oberto et al.[17] using the same animal model (Eμ-*pim*-1). The investigators used restraints on the animals to achieve uniform exposure levels, from the pulsed 900 MHz, signal. The mice were exposed to whole body SAR values of either 0.5, 1.4, or 4.0 W/kg, or to sham exposure for one hour per day, 7 days per week for the duration of the study, with complete histologic examination of all mice. Compared to the sham-exposed controls, the RF-exposed animals had lower survival, which was statistically significant in the male mice but not in the female, and without an exposure-response gradient. However, no differences in lymphoma incidence were seen between the RF- and sham-exposed mice. The authors concluded that the results did not support a role of RF exposure in carcinogenesis.

A further study was completed by Sommer et al. (2007)[18] in a different mouse strain (AKR/J mouse) which develops leukemia/lymphoma as a result of incorporation of a virus into its genome rather than a transfected oncogene (cancer causing gene) as in the Eμ-*pim*-1 mouse. One hundred sixty (160) AKR/J mice in each study arm were either exposed or sham-exposed to a UMTS test signal (around 1950 MHz modulated at 1.6 GHz and designed to simulate UMTS power control in mobile phone calls) 24 hours per day for 248 days. Animals were unrestrained but were housed in an

elaborate metal mesh and perspex grid system which ensured even RF exposure. Results showed no differences in leukemia-lymphoma incidence or survival time between exposed and sham-exposed mice. Results seen in this study were the same as those seen in an earlier investigation by the same group in 2004[19] using a 900 MHz pulsed GSM signal instead of 1966 MHz UMTS.

Saran and colleagues (2007)[20] exposed newborn *Patched1* heterozygous knockout mice and their wild-type siblings to a uniform plane-wave 900 MHz GSM signal at a SAR of 0.4 W/kg or sham for 30 minutes twice per day for five days to determine whether RF fields increased risk of medulloblastoma, a type of brain tumour. The *Patched1* animal was chosen for this study because it is susceptible to development of medulloblastoma. No differences in tumour incidence or overall survival were seen between the exposed and sham-exposed groups at the end of the study. The authors concluded there was no evidence of a carcinogenic effect on the central nervous system (CNS) due to neonatal exposure to 900 MHz fields in this susceptible animal model after the 48-week duration study. It would appear that no other long-term assays have used this animal model, so no replication has been attempted.

Lee et al. (2011)[21] exposed AKR/J mice to the effects of both CDMA and WCDMA RF fields simultaneously. Six-week-old mice were exposed to 848 MHz CDMA and WCDMA carrier signal at 1950 MHz in a reverberation chamber for 45 minutes per day, five days per week for up to 42 weeks. SAR values for each exposure were 2.0 W/kg, 4 W/kg in total. A group of animals were sham exposed in the same chambers as part of the protocol. Comparison of lymphoma rates among groups at the end of the study revealed no significant difference between rates in the dual RF-exposed mice compared to the sham-exposed animals. The authors concluded that the results did not indicate a relationship between RF fields and lymphoma.

A series of studies were carried out prior to 2005 to evaluate whether C3H MMTV+ mice exposed to RF fields had a higher incidence of mammary tumours (data not tabulated).[22-25] This mouse carries the mouse mammary tumour virus and is highly susceptible to mouse breast tumours. After groups of mice were exposed by different researchers to RF fields for 16,[25] 18,[22,23] and 21[24] months duration, none showed any increased risk of mammary tumours by comparison with sham-exposed mice.

Table 2. Cancer and RF field exposure in tumour-prone animal models

Study	Animal Species/ Strain	Exposure	Tumour	Results	Comments
Utteridge et al. (2002)[16]	Eμ-pim-1 female mice	898 MHz GSM-pulsed signal; SAR 0.25–4.0 W/kg, 1 hr per day, 5 days/wk, up to 104 wks	Lymphoma	No significant difference in lymphoma incidence between RF-exposed mice at any SAR level and sham-exposed mice	Did not replicate Repacholi et al. (1997)[15] results
Oberto et al. (2007)[17]	Eμ-*pim*-1 mice	900 MHz pulsed at 217 HZ, 0.6 ms; SAR 0.5, 1.4, 4.0 W/kg or sham, 1 hr/day, 7 days/wk for 18 mos	Lymphoma	No difference between RF- and sham-exposed mice in lymphoma incidence	Mortality higher in RF-exposed groups than in control groups at SAR 0.5 W/kg but not at higher levels
Sommer et al. (2007)[18]	AKR/J female mice	UMTS 1.966 MHz; power control jumps; SAR 0.4 W/kg, or sham, 24 hr/day, 7 days/wk for 35 wks	Lymphoma	No difference in lymphoma incidence between RF- and sham-exposed mice	RF exposure had no effect on overall animal survival
Saran et al. (2007)[20]	Patched 1 hetero-zygous knock-out and wild-type mice	900 MHz; GSM; SAR 0.4 W/kg or sham for 0.5 hr 2x/day post natal day 2 thru 6	CNS tumours	RF-EMF had no effect on incidence of cerebellar tumours, basal cell carcinoma-like phenotype of rhabdomyo-sarcoma	No evidence that RF-EMF exposure affected survival in either $Ptc^{\pm}$ or wild-type mice
Lee et al. (2011)[21]	AKR/J mice	Combined CDMA (849 MHz) and WCDMA (1950 MHz); SAR 4.0 W/kg total for 45 min/day, 5 days/wk for 42 wks	Lymphoma	No increase in lymphoma in mice exposed to combined CDMA and WCDMA vs. sham-exposed mice	RF exposure had no effect on overall survival

6B.4.3 Cancer initiation/promotion and RF exposure

Another group of studies has been carried out using rats and mice to examine the possibility that RF might promote the development of cancer in animals previously exposed to a known carcinogen. These studies examine the effect of mobile phone RF field exposure in comparison to sham exposure on the incidence of tumours of the brain or central nervous system (CNS) chemically induced by N-ethylnitrosourea (ENU) and mammary tumours induced by 7, DMBA.

6B.4.4 CNS tumours (Table 3)

Shirai and colleagues (2005)[26] conducted a study to assess whether RF fields would increase the incidence of CNS tumours in Fischer 344 rats exposed in utero to 4 mg/kg of N-ethyl-N-nitrosourea (ENU), a potent mutagen and carcinogen, by comparison to mice exposed to the same chemical agent but not to RF fields. Rats were exposed to a 1439 MHz TDMA near field signal at SAR of 0.67 or 2 W/kg for 90 minutes per day, five days per week for 104 weeks or sham. A cage control group exposed neither to ENU nor to RF fields was also included. At the end of the study, surviving animals were euthanized and all animals, including those dying during the course of the study were histopathologically examined with the pathologist blind to the exposure status of animals. Results showed no increase in CNS tumour incidence in either the low or high RF+ENU rats by comparison to the rats with ENU and sham exposure. In addition, no effects were seen on levels of a number of important hormones, including ACTH, corticosterone or melatonin in RF+ ENU-exposed animals compared to those with sham exposure plus ENU.

Zook and Simmens (2006)[27] examined the possibility that RF exposure to Sprague-Dawley rats might increase risk of CNS tumours induced by 6.25 or 10 mg/kg ENU administered in utero. Rats were exposed to pulsed 860 MHz RF fields or sham in restraints in a “ferris wheel” exposure set-up, beginning on day 53 after parturition, for six hours per day, five days per week for between 171 and 325 days. At the end of 24 months, all surviving rats were killed and examined. No increase in incidence, multiplicity or latency of any type of CNS tumour was seen by addition of RF field exposure to either rats exposed to 6.25 mg/kg or 10 mg/kg of ENU by comparison to rats exposed to identical doses of ENU with sham RF exposure.

In 2007 Japanese investigators[28] evaluated the effect of exposure to 1950 MHz W-CDMA RF near field exposure (equivalent to that with use of a hand-held mobile phone on an IMT-2000 system) for two years on CNS tumour development after exposure to 4 mg/kg of ENU in utero. The study was similar to an earlier negative investigation conducted by the same research group using a Japanese mobile phone 1439 MHz TDMA signal.[26] A total of 500 Fischer 344 rat pups were divided into several groups treated with ENU alone, ENU plus RF at SAR levels of 0.67 or with 2 W/kg to the brain, or ENU and sham RF exposure. A fifth group comprising cage controls was also included in the protocol. Exposure to RF fields began at five weeks, 90 minutes per

day, five days per week for 104 weeks. Rats were restrained in tubes during exposure in order to ensure accurate RF exposure to the brain. At the end of the study, no significant increases in tumour incidence were seen in either males or females in the RF-EMF-exposed groups of rats by comparison with rats exposed in utero to ENU + sham exposure. In addition, no significant differences were seen in ACTH levels or levels of melatonin in RF-EMF-exposed animals compared to non-exposed. Two earlier 24-month studies by Adey and colleagues[10,29] using Fischer 344 rats exposed to in utero ENU and to 836 MHz fields also showed no increase in incidence of CNS tumours.

6B.4.5 Mammary and liver tumours (Table 3)

Several investigations have been conducted to examine the possible promotional effect of mobile phone RF signals on the incidence of rat mammary tumours (the rat analogue of breast cancers in women) induced by 7, 12-dimethybenz(a)anthracene (DMBA), a potent carcinogen and mutagen.

The study by Yu and colleagues (2006)[30] involved dividing 500 Sprague-Dawley rats into four groups which were initially treated with 35 mg/kg of DMBA. Three groups were then exposed to 900 MHz GSM signal with whole body SAR levels of 0.44, 1.33, or 4.0 W/Kg in an exposure wheel and a fourth comprising a control group with sham exposure. A cage control group treated with neither DMBA nor RF exposure was also included. RF field exposure commenced at day 48, the day after DMBA administration, and continued for four hours per day, 5 days per week for 26 weeks. At study completion, all animals were euthanized and necropsied. All pathologic examination (and RF exposure) was conducted with investigators blind to the exposure status of the animals. There were no significant differences in mammary tumour incidence between the sham-exposed controls and any of the GSM-exposed rat groups, nor any differences in time to tumour onset, or multiplicity, or size of tumours.

Mammary cancer incidence was examined in 500 DMBA-treated Sprague-Dawley rats divided into five groups, with three being administered increasing levels of exposure to pulsed 902 MHz fields giving SAR values of 0.44, 1.33, or 4.0 W/Kg for four hours per day, five days per week, for six months.[31] A fourth group was sham-exposed, and a cage control group was incorporated into the protocol. During exposure, the rats were restrained in polycarbonate tubes placed in a “ferris wheel” exposure set-up to ensure uniformity of RF fields throughout the study. During the course of the study, all animals were examined weekly to detect mammary tumours. At the end of the study, all remaining animals were sacrificed and pathologic examination of animals was conducted.

At the conclusion of the study, the rats with the highest SAR levels (4.0 W/Kg) from exposure to 900 MHz fields had developed a greater number of malignant mammary tumours than rats with lower SARs, but lower numbers of benign tumours. No dose–response gradient from lowest to highest SAR was seen, and in addition, the cage control animals without exposure to RF-EMF developed essentially the same number of

malignant mammary tumours as the rats in the highest exposure group, and even more benign tumours. The inconsistency of the results and lack of a dose-response gradient led the authors to conclude that the differences seen between the groups of animals were incidental and not attributable to RF-EMF exposure. Earlier studies by Bartsch et al. (2002)[32] and by Anane and colleagues (2003)[33] using Sprague-Dawley rats with mammary tumours induced by DMBA also demonstrated no role for 900 MHz pulsed GSM exposure in increasing incidence of the tumours.

No recent studies have evaluated liver tumours, but in an older Japanese study (1998),[34] unrestrained Fischer 344 rats were exposed to pulsed 929 MHz near field signal (SAR of between 1.9 and 0.9 W/kg at the liver) or sham for 90 minutes per day, five days per week for six weeks. The rats had previously been given a single dose of diethylnitrosamine (DEN) at six weeks of age. In addition, three weeks after commencement of RF exposure, all rats had a 2/3 partial hepatectomy. Six weeks after RF exposure began, animals were euthanized and examined for pre-neoplastic lesions in the liver by comparing the numbers and areas of the induced glutathione S-transferase placental form (GST-P)-positive foci in the livers of exposed and sham-exposed rats. No significant differences were seen between the RF- and sham-exposed groups. A further study by the same group[35] with Fischer rats but using 1439 MH TDMA signal instead of 929 MHz signal with the same exposure schedule as noted above, again found no indications that the RF fields promoted the induction of pre-neoplastic lesions in the liver.

6B.4.6 Skin tumours (Table 3)

Several recent bioassays evaluating the promotional effects of RF-EMF on skin cancers have been carried out fairly recently in mice.

A study by Huang and colleagues (2005)[36] using ICR mice examined whether RF exposure promoted skin tumours initiated by DMBA. Mice were shaved and given a single topical application of DMBA (100 μg/100 μl acetone per mouse). They were then randomized into four groups with exposure to a CDMA signal at 848.5 MHz, or 1762.5 MHz, or sham. A fourth group was exposed to 12-O-tetradecanoylphorbol-13-acetate (TPA) as a positive control group. The addition of positive controls, that is, a group in which it is certain that skin tumours will develop, can assist investigators in knowing what type of tumour to assess from DMBA and RF exposure. The maximum whole body SAR was 2.4 W/kg at 849 MHz and 12.2 W/Kg at 1763 MHz, but the average whole body exposure during the course of the study was 0.4 W/Kg. The RF schedule was two cycles of 45 minutes RF exposure, 15 minutes apart, five days a week, for 19 weeks. Although the TPA positive control group developed skin cancers as expected, no indication was found at the termination of the study after 20 weeks that either of the DMBA + RF-exposure mice or the sham-exposed group developed skin tumours or showed any perturbations in skin cell proliferation. The results indicate that DMBA and RF fields did not act together as co-carcinogens in genesis of skin cancer.

One other recent study by Paulraj and Behari (2001)[37] evaluated RF exposure in conjunction with DMBA in the generation of skin tumours (papillomas) in Swiss albino mice. Mice were divided into seven groups, one control, one with DMBA (100 µg) application only, groups with DMBA plus either 112 MHz RF amplitude modulated at 16 Hz (SAR of 0.75 W/kg) or 2450 MHz radiation (SAR of 0.10 W/kg), one with 112 MHz RF exposure only, and one with 2450 MHz exposure only. A seventh group acted as a positive control with application of DMBA plus croton oil. RF exposure for two hours per day, three days per week, was continued for 16 weeks. At study termination, skin tumours were seen only in the positive control group. No effect was seen with exposure to either 112 MHz or 2450 MHz fields alone or in combination with DMBA.

Table 3. Cancer initiators/promoters and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Initiator/ Co-carcinogen	Tumour	Result	Comments
	CNS Tumours					
Shirai et al. (2005)[26]	Fischer 344 Rats	1439 MHz TDMA; SAR 0.67 or 2.0 W/kg to brain, or sham; 90 min/day, 5 days/wk for 104 wks	ENU in utero 4 mg/kg	CNS tumours	No signifi-cant increase in CNS tumours in RF-exposed vs. sham- exposed rats	No effect of RF exposure on ACTH, corticos-terone or melatonin levels
Zook and Simmens (2006)[27]	Sprague-Dawley rats	Pulsed 860 MHz signal; brain SAR 1.0 ± 0.2 W/kg or sham; 6hrs/day, 5 days/wk for 171–325 days	ENU at 6.25 or 10.0 mg/kg	CNS tumours	No effect on CNS tumour incidence malig-nancy, volume multipli-city latency	
Shirai et al. (2007)[28]	Fischer 344 Rats	1950 MHz W-CDMA signal; SAR 0.67 or 2.0 W/kg to brain or sham; 90 min/day, 5 days/wk for 104 wks	ENU in utero 4 mg/kg	CNS tumours	No effect of RF on incidence of CNS tumours	No effect of RF on ACTH, corticosterone or melatonin levels
	Mammary Tumours					
Yu et al. (2006)[30]	Sprague-Dawley female rats	900 MHz; SAR levels of 0, 0.44, 1.33, 4.0 W/kg, or sham; 4 hrs/day, 5 days/wk for 26 wks	Single dose of DMBA 35 mg/kg	Mammary tumours	No statistically significant elevation or reduction in mammary tumours in any RF- exposure group	
Hruby et al. (2008)[31]	Sprague-Dawley rats	902 MHz pulsed signal; SAR 0.4, 1.3, or 4.0 W/kg or sham; 4 hrs/day, 5 days/wk for 6 mos	Single dose of DMBA	Mammary tumours	More malignant tumours in highest SAR RF group than mid or low but about same as the cage controls. No dose-response gradient by RF dose	Authors noted that differences between RF groups are incidental rather than attributable to RF exposure

Study	Animal Species/ Strain	Exposure	Initiator/ Co-carcinogen	Tumour	Result	Comments
	Liver Tumours					
Imaida et al. (2001)[35]	Fischer 344 rats	1439 MHz near field TDMA; SAR liver 0.9–1.37 W/kg, 90 min/day, 5 days/wk for 6 wks	DEN 200 mg/kg + partial hepatectomy	Pre-neoplastic liver lesions	1439 MHz RF does not promote liver cancer	
	Skin Tumours					
Huang et al. (2005)[36]	ICR mice	849 MHz or 1763 MHz CDMA real signal or sham (whole body SAR 0.4 W/kg); 90 min/ day, 5 days/wk for 19 wks	10 µg dose of DMBA at 7 wks for all mice	Skin tumours	No joint effect of exposure to 849 or 1763 MHz + DMBA on incidence of skin cancers	
Paulraj and Behari (2011)[37]	Swiss albino mice	112 MHz AM signal at 16 Hz or pulsed 2450 MHz or sham; 2 hrs/day for 14 wks	Single dose 100 µg DMBA; DMBA and croton oil as positive control	Skin tumours	No effect of 112 MHz or 2450 MHz RF alone or with DMBA on skin tumour genesis	

Summary

Long-term bioassays have long been considered the "gold standard" for investigations of carcinogenicity in animals. Studies conducted using RF field exposure alone as a tumour-initiator have been convincingly negative even with exposures of two years. Further, these studies have exposed rats and mice to RF levels over the course of the animals' lives, which substantially exceed levels seen in humans. The animal evidence therefore would indicate that it is very unlikely that RF exposure alone would be carcinogenic to humans.

The investigations of RF radiation as a tumour promoter in conjunction with known carcinogens have also been negative, and again, at levels above those seen in day-to-day human exposure.

The studies cited in this review are of very high quality. Most feature full microscopic assessment of multiple tissue samples in experimental animals, with the pathologist "blind" to the exposure status of the animals. They also include accurate RF dosimetry, with animals either restrained during exposure to ensure precise SAR levels in specific tissues or exposed in reverberation chambers to allow movement while preserving accurate whole body SARs. The lack of any body of evidence showing a strong association between any tumour and RF exposure, the lack of dose-response relationships, and the lack of analogous findings with human cancer in the epidemiologic data, all important criteria for causal associations[38] militate against any suggestion that RF field exposure alone initiates or promotes the growth of cancer in animals. Repacholi et al. (2012)[39] in a recent comprehensive review including bioassay results for cancers of the central nervous system, found no compelling evidence of RF radiation carcinogenicity in animal studies.

6B.5 Toxicologic Studies and RF Exposure

6B.5.1 DNA damage and RF exposure (Table 4)

An early study by Lai and Singh (1996)[40] exposed Sprague-Dawley rats to 2450 MHz pulsed or continuous wave RF fields or sham for two hours at 1.2 W/kg whole-body SAR. On examination of brain tissue immediately after exposure, an increase in both single- and double-strand DNA breaks were seen in the animals exposed to pulsed or continuous wave RF compared to sham-exposed rats. A similar experiment, conducted by the same investigators in 2004[41] exposed rats to either a 2450 MHz field alone, a temporarily incoherent magnetic field alone, both exposures together or sham and again found higher levels of single and double strand DNA breaks in rats exposed solely to 2450 MHz fields than sham-exposed rats; however, those exposed to both the RF fields and the temporarily incoherent magnetic field appeared to have no more DNA breaks than sham-exposed animals.

An attempt was made by a European group, specifically Verschaeve et al. (2006),[42] to replicate the results of Lai and Singh (1996)[40] using Wistar rats exposed to pulsed 900 MHz GSM signal for two hours per day for a period on 24 months (SAR 0.4 W/kg), for two hours per day, five days per week for 24 months. In addition, the animals were also exposed to the potent mutagen/carcinogen 3-chloro-4-(-dichloromethyl)-5-hydroxy-2(5H)-furanone (MX) in their drinking water throughout the study. Other rats were exposed to MX alone. Double-strand DNA breaks were analysed using the alkaline Comet assay. The Comet assay assesses DNA damage by applying pulsed gel electrophoresis to DNA extracted from test animals. This results in a “comet like” figure as negatively charged DNA fragments migrate toward the positive pole. The amount of DNA in the “comet tail” is used as the measure of DNA damage. In rats exposed to MX, damage was seen, as expected, in blood liver and brain cell DNA, but in the rats exposed to the 900 MHz radiation as well as MX, no increase was seen in DNA damage over MX alone. The authors concluded that the results provided no indication that RF fields enhanced MX DNA damage.

Belyaev and colleagues (2006)[43] also attempted to replicate the results of the 1996 study[40] by Lai and Singh. Fischer 344 rats were exposed to 915 MHz GSM signal at a whole body SAR of 0.4 W/kg or sham in a transverse electromagnetic transmission (TEM) cell for two hours. Use of the TEM cell enabled accurate whole body exposure while allowing animals to move around. At the conclusion of the study, examination of brain cells found no evidence of increased DNA double-strand breaks by comparison with sham exposed rats.

Micronucleus formation and chromosomal aberrations are indications of DNA damage, and several studies have evaluated micronucleus formation in tissues of animals exposed to RF fields. Ferreira and colleagues[44] exposed pregnant Wistar rats to 834 MHz RF signal for 8.5 hours from gestation to birth at SAR values of 0.55–1.23 W/kg or

sham. At birth, the animals were sacrificed and an increased level of micronucleus formation was seen in the bone marrow of RF-exposed versus sham-exposed animals.

The joint Belgian-Finnish study noted above[42] also assessed micronucleus formation but found no increased formation in rat brain and liver samples of the RF-exposed animals by comparison with those exposed to MX alone. Gurbuz et al. (2010)[45] exposed Wistar rats to an 1800 MHz modulated GSM signal applied 20 minutes per day, five days per week for one month and found no increase in micronucleus formation in exfoliated bladder cells from rats exposed to the RF fields by comparison with control rats.

Table 4. Toxicologic changes and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Results	Comments
Lai and Singh (1996)[40]	Sprague-Dawley rats	2450 MHz pulsed or CW signal; SAR 1.2 W/kg or sham for 2 hrs	Increased single- and double-strand breaks in RF- exposed rat brain	
Lai and Singh (2004)[41]	Sprague-Dawley rats	2450 MHz CW signal; SAR 0.6 W/kg; or 45 mG magnetic field, or both, or sham for 2 hrs	Increased single- and double-strand DNA breaks in RF-exposed rat brain	Increase in DNA breaks in RF-exposed rats attenuated by concurrent magnetic field
Verschaeve et al. (2006)[42]	Wistar rats	900 MHz pulsed signal; SAR 0.3 or 0.9 W/kg + 19 µg/ml MX mutagen in water or MX and sham RF exposure; 2 hrs/day, 5 days/wk for 24 mos	No increased DNA damage in brain and liver tissue of rats exposed to RF and MX compared to MX alone; no increase in micronuclei	
Belyaev et al. (2006)[43]	Fischer 344 rats	915 MHz GSM signal pulsed SAR 0.4 mW/g or sham for 2 hrs	No increased DNA damage in RF-exposed rat brain cells than sham-exposed	
Ferriera et al. (2006)[44]	Wistar rat pups	834 MHz; SAR 0.55-1.23 W/kg; 8.5 hrs/day from gestation to birth or sham	Increased erythrocyte micronucleus formation in RF-exposed pups	
Gurbuz et al. (2010)[45]	Wistar rats	1800 MHz GSM pulsed signal for 20 min/ day, 5 days/wk, for 1 mo or sham	No increased micronuclei in exfoliated bladder cells in RF vs. control animals	

6B.5.2 Reactive oxygen species and RF exposure

Production of reactive oxygen species occurs in normal physiological processes involving oxygen. While small levels of reactive oxygen species have a role in physiologic processes such as apoptosis, they also contain free radicals which, at high concentrations, can damage DNA.

Two studies[46,47] exposed female Wistar rats to pulsed 900 MHz or sham exposure for 30 days and showed increased levels of malondialdehyde in the endometrium of exposed rats. Malondialdehyde is a molecular indicator of lipid peroxidation which generates reactive oxygen species. Of interest, the authors noted that increasing levels of vitamin C or E in the diet appeared to ameliorate potentially damaging reactive oxygen species. Most studies of reactive oxygen species with RF exposure are conducted using cellular model systems rather than animals, and these investigations are outlined in Section 6A (Cellular Studies).

6B.5.3 Apoptosis and RF exposure (Table 5)

Apoptosis, or programmed cell destruction, is a process whereby a cell initiates a process of self-destruction when significant toxic or genetic damage accumulates. While the normal process of apoptosis ensures that an animal (or human) retains healthy cells, the appearance of significant numbers of apoptotic cells in experimental animals may indicate dangerous conditions for cell survival. Dasdag and colleagues[48] exposed Wistar rats to either 900 MHz GSM signal at SAR levels from 0.17–0.58 W/kg or sham two hours per day, 7 days per week for 10 months to look for signs of apoptosis in brain cells or indications of increase in reactive oxygen species. Cage control animals were included in the study as well as the sham rats. Apoptosis scores in the RF-exposed animals proved to be lower than those in the sham-exposed or cage control rats. In addition, no significant differences were seen between the three groups in oxidative stress index levels.

A rabbit animal model was also used to evaluate apoptosis levels after exposure to RF fields.[49] Two strains (California and New Zealand rabbits) were exposed to 650 MHz broadcast signal or sham 24 hours per day for a period of two years. After two years exposure, some RF-exposed animals were sacrificed immediately and some were retained for another 1.5 years post-exposure prior to killing. Results of examination of brain tissue showed an increased number of apoptotic cells in the animals exposed to RF fields and sacrificed after 24 months exposure, and a further increase in such cells in rabbits left for a further 1.5 years before sacrifice, compared to sham and cage control animals.

Investigators in Korea exposed C57BL mice to RF fields at 849 MHz and 1763 MHz (as used in a Korean mobile phone system) or sham for one hour per day, five days per week for periods of up to one year.[50] Exposure was conducted with animals restrained in order to ensure good control of exposure to the brain. At six months and at one year, groups of exposed and sham mice were humanely killed and brain tissue examined. No indications of increased apoptotic cells were seen in RF-exposed vs. sham-exposed animals.

French[51] and Japanese scientists[52] conducted studies of RF exposure in Fischer 344 rats exposed to 900 MHz and 915 MHz GSM fields respectively. Both studies were designed to evaluate blood-brain permeability and are described in detail in the following

section; however the results of both studies showed no increases in indicators of apoptosis in the brain cells of RF-exposed rats compared with sham-exposed animals.

Table 5. Apoptosis and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Result	Comments
Dasdag et al. (2009)[48]	Wistar rats	900 MHz GSM signal; SAR 0.17-0.58 W/kg or sham; 2 hr /day, 7 days/wk for 10 mos	Decrease in apoptosis in RF-exposed rats.	
Tarantino et al. (2005)[49]	California and New Zealand rabbits	650 MHz broadcast signal; SAR 3.4 W/kg or sham; 24 hrs/day for 52 wks	Increase in apoptotic cells in brain tissue of RF-exposed vs. sham-exposed animals	Dosimetry description is confusing
Kim et al. (2008)[50]	C57BL mice	849 MHz or 1763 MHz signal; SAR 7.8 W/kg; or sham; 1 hr/day, 5 days/wk for 6 or 12 mos	No indications of increased cell apoptosis in RF-exposed animals compared to sham	
Poulletier de Gannes et al. (2010)[51]	Fischer 344 rats	915 MHz GSM signal; SAR 0.14 or 2.0 W/kg for 2 hrs or sham	No apoptotic neurons detected	
Masuda et al. (2009)[52]	Fischer 344 rats	915 MHz GSM signal; SAR levels of 0.02, 0.2, or 2.0 W/kg or sham for 2 hrs	No increase in apoptotic cells in RF-exposed vs. sham-exposed rats	Followed closely the protocol of Salford et al., 2003

6B.5.4 Gene expression and RF exposure (Table 6)

Studies of gene expression in animals are designed to determine whether exposure to RF fields alters the way in which genes code for production of polypeptide chains and ultimately proteins in living animal systems. Genes and their expression ultimately control processes such as cell differentiation and proliferation and cell death, organ structure, and other functions in animals and humans. Although gene expression changes may not all be considered genotoxic, they are grouped here with other toxicologic studies for convenience.

Belyaev and colleagues (2006)[43] used an Affymetrix U34A gene chip to probe some 8800 genes to evaluate expression changes in the brains of eight Fischer 344 rats exposed for two hours to pulsed 915 MHz signal at a whole body SAR of 0.4 W/kg. Gene chips such as the Affymetrix device used in this study hold DNA probes from one of DNA's double helices, and these can recognize the corresponding DNA from the other helix in experimental samples. The chips allow analysis of a large number of potential gene variants quickly and at relatively low cost. On analysis, the study found 11 up-regulated genes and one down-regulated. The genes were reported as encoding for a variety of functions including neurotransmitter regulation as well as blood-brain barrier permeability and melatonin production. The authors noted that because of the small number of rats used in the study and the limited power, the results should be treated cautiously.

Finnie (2005)[53] exposed C57BL/6NTac mice to pulsed 900 MHz GSM signals or sham for a period of 60 minutes. After the exposure, brains of the animals, in addition to those of a cage control group of mice, showed no greater c-*fos* (a marker of neuron activity) expression among mice subjected to acute exposure to short-term RF fields compared to sham-exposed mice. The exposed and sham mice were restrained during exposure, however, and analysis showed higher levels of *c-fos* expression in the restrained animals (RF- and sham-exposed) than in cage controls, suggesting that stress levels in animals may be a potential confounder in gene or protein expression studies.

The same group[54] followed their earlier study with an assessment of longer-term exposure to pulsed 900 MHz fields using similar methods to those in the 2005 investigation described above. C57BL/6Ntac mice were exposed 60 minutes per day, five days per week, for 104 weeks and showed no effect of RF field exposure on *c-fos* expression in the brain by comparison with the sham exposed mice.

Paparini and colleagues (2008)[55] evaluated gene expression in the brain tissue of Balb/cJ mice using the Affymetrix Mouse Expression Array 430A (a chip which includes more than 14,000 mouse gene probes) after a single one-hour exposure to 1800 MHz GSM radiation (average brain SAR 0.2–0.56 W/kg) or sham exposure in a transverse electromagnetic (TEM) cell (a device which ensures a consistent and uniform RF frequency field). The investigators conducted a preliminary analysis using as a cut-off point a greater than 1.5-fold increase or decrease in expression by comparison with that expected, and showed that 301 probes were differentially expressed in the RF-exposed mice. However, they determined that a more stringent analysis was necessary because the many comparisons made between normal and test values would produce a significant number of false-positive findings due to chance alone. After the more stringent analysis, the authors concluded that no significant differences in gene expression were found between the RF-exposed and sham-exposed animals.

A further evaluation by Finnie and colleagues (2009)[56] was conducted to see whether exposure to RF fields in utero might induce a stress response in the brains of fetal mice as indicated by induction of heat shock proteins Hsp32 or Hsp70. Pregnant Balb/c mice were exposed to a 900 MHz GSM field 60 minutes per day for the entire gestational period of 19–20 days at a SAR level of 4.0 W/kg. At gestation, the pups were killed and their brains were analysed, but no differences were seen in Hsp32 and Hsp70 in the RF- versus sham-exposed mice.

Taken together, the literature has produced some indications that RF exposure might cause gene expression changes in animals exposed to such fields, but most studies did not. Replication of the positive studies has been lacking, and even where changes in expression level appeared to occur, these changes have not yet been shown to result in change in gene function. With increasing use of high-throughput techniques for gene expression studies in future, there is a potentially high false discovery rate[57,58] as some genes will be over- or under-expressed by chance alone. However, researchers

working in this area are aware of this issue and appear to be adjusting their statistical testing procedures to minimize false positives.

Table 6. Gene expression and RF field exposure in animal models

Study	Animals Species/Strain	Exposure	Result	Comments
Finnie et al. (2005)[53]	C57BL/6NTac mice	900 MHz pulsed signal; SAR 4 W/kg (whole body) or sham for 1 hr	*c-fos* expression in brain same in RF- and sham-exposed mice	Cage control arm had lower expression of *c-fos* in brain compared to RF and sham arms
Belyaev et al. (2006)[43]	Fischer 344 rats	915 MHz GSM pulsed signal; SAR 0.4 W/kg or sham for 2 hrs	11 up-regulated and 1 down-regulated gene in brain tissue	
Finnie et al. (2007)[54]	C57BL/6NTac mice	900 MHz pulsed GSM signal; SAR 4 W/kg (whole body) or sham; 1 hr/day 5 days/wk, for 104 wks	*c-fos* expression in brain tissue same in RF- and sham-exposed mice	Cage control (unrestrained) animals had lower *c-fos* expression than RF and sham arms
Paparini et al. (2008)[55]	Balb/cJ mice	1800 MHz GSM signal SAR (brain) 0.2–0.56 W/kg or sham for 1 hr	No consistent evidence of gene expression modulation by RF field exposure in brain tissue	
Finnie et al. (2009)[56]	Balb/C mice	900 MHz pulsed GSM signal in utero SAR 4 W/kg or sham; 60 min/day for 19–20 days	No difference in induction of Hsp32 or Hsp70 in RF-compared to sham-exposed mice	

Summary

The recent studies of putative toxicological changes due to RF radiation in animals have been characterized by superior means of animal restraint to control RF exposure to specific organs, better control of thermal effects, and better descriptions of experimental protocols than studies published prior to 2004–2005. Characterization of RF dosimetry is still a weak point only in a few studies. However, these improvements have not contributed to more consistent evidence for an effect of RF exposures on physiological processes in animals. Results of studies of DNA damage, micronucleus formation, apoptosis, production of reactive oxygen species, gene expression changes, and other genotoxic effects carried out using RF exposure of animal models (mice and rats) tend to be contradictory. Positive results found in one species are usually not replicated. Overall, the criteria important in establishing a causal relationship between short-term or long-term RF exposure and changes in gene expression, apoptosis, production of reactive oxygen species and other potential biologic changes in animal physiology are lacking. Such criteria include consistency of results over several studies among similar animals and strong associations between exposure and response with control for potential confounding factors. This lack of consistent evidence reduces the likelihood that significant adverse physiologic effects occur in animal models due to RF exposure.

6B.6 Central Nervous System and RF Exposure

6B.6.1 Blood- brain barrier and RF exposure (Table 7)

A number of experimental studies have been conducted in animal models to determine whether exposure to RF fields alters the permeability of the blood-brain barrier. The presence of very tight junctions between endothelial cells in central nervous system capillaries serves to restrict access to the brain of bacteria and other substances to a much higher degree than in other organs of the body. Integrity of this barrier is one of the reasons that bacterial infections in the brain are rare. Reduction in tightness of this barrier, if caused by RF field exposure, could therefore have significant adverse health effects in humans.

Initial concern was raised by a study conducted by a group of scientists from Lund University in Sweden in 1994.[59] In 2003 the Swedish group[60] exposed Fischer 344 rats 12–26 weeks of age to 915 MHz continuous wave and pulsed GSM signal or sham exposure for a period of two hours in a TEM cell at three SAR levels (2, 20 or 200 mW/kg). After exposure, the rats were observed for 50 days and sacrificed. Examination revealed increased permeation of albumin from capillaries into both white and grey brain matter in RF-exposed rats by comparison with sham-exposed animals, suggesting that exposure to pulsed RF fields at around 900 MHz increases permeability of the blood-brain barrier. They also observed an increase in "dark neurons," indicators of neuronal damage in rat brains in animals exposed to RF fields.

The latest study by the Swedish group (2009)[61] investigated the effect of RF exposure on Fischer rats in a TEM cell. The rats were divided into groups and were exposed to a 900 MHz GSM signal from a mobile phone at SAR levels of 0.0012, 012, 0.12 W/kg or sham for a period of two hours. After a recovery period of seven days, the animals were sacrificed and necropsied. The investigators found significant foci of albumin leakage in grey and white matter surrounding capillaries in the rats exposed to 0.012 W/kg. More modest levels of extravasation were seen at other SAR levels.

Finnie and colleagues in Australia (2006)[62,63] initiated several studies to see if younger animals might be more sensitive to potential blood-brain barrier permeability with exposure to RF fields. Balb/c mice were exposed to 900 MHz GSM pulsed RF signal or sham 60 minutes per day either in utero (gestational days 1–19) or for seven days after birth. The protocols included cage control and a positive control group which had had a single injection (2 mg/kg) of cadmium chloride, a substance known to disrupt the blood-brain barrier. Although extravasation was seen in the brains of the positive control animals, no indications of increased albumin extravasation were seen in either in utero or early life RF-exposed mice by comparison with sham and cage control animals.

An investigation by Turkish scientists (2009)[64] also reported leakage. Their study utilized a Wistar rat model with exposure to 900 or 1800 MHz continuous wave near

field signal or sham for a period of 20 minutes at 12.6 V/m. No SAR value was given in the paper. Evans blue dye was employed as a tracer material injected into tails of the rats 20 minutes prior to RF exposure. Brains of the rats were examined immediately after RF exposure and leakage of Evans blue stain into the brain in male (but not female) rats was seen with exposure to 900 or 1800 MHz signal. It is not clear why significant differences in permeability were seen between exposed and sham male rats, but similar findings were not seen in female rats.

The Japanese study of Masuda et al. (2009)[52] exposed Fischer 344 rats to 915 MHz pulsed fields at SARs up to 2.0 W/kg or sham for a period of two hours in a TEM cell following as closely as possible the protocol described by Salford et al. (2003).[60] Separate cold and chemical injury rats were also included in the protocol as positive controls. At days 14 and 50, RF-exposed and sham rats were sacrificed and their brains evaluated. No elevated levels of extravasation or "dark neurons" were seen in RF-exposed rats compared to sham-exposed controls. The authors reported that the results failed to confirm the Swedish study.

An American study (2009)[65] exposed Fischer 344 rats to 30 minutes of 915 MHz continuous wave and 915 MHz pulsed wave RF fields at SARs from .0020–20 W/kg or sham in TEM cells. Animals were restrained during exposure in order to ensure good control of RF exposure to the brain, and positive brain injury controls as well as cage control rats were included in the protocol. After examination of the brains of all the animals, no increases in extravasation were found in any of the RF-exposed groups by comparison with sham-exposed or cage control rats.

Poulletier de Gannes and colleagues in France (2010)[51] conducted a very similar study to that of Salford et al. (2003)[60] using Fischer rats exposed to 915 MHz GSM for two hours at SARs of 0.14 W/kg, or 2 W/kg or sham. This study also optimized RF exposure to the brain using animal restraints, resulting in very precise RF exposure. The study included cage controls as well as cold injured positive controls. After 14 and 50 days the rats were killed and brains examined. Again no evidence of leakage across the blood-brain barrier was seen in RF-exposed rats by comparison with sham-exposed animals.

Finnie et al. (2009)[66] exposed mice to 900 MHz pulsed far field RF at SAR of 4 W/kg or sham for 60 minutes per day, 5 days per week for a much longer period of time than previous studies (104 weeks). Cage control and chemical brain-injured (clostridium toxin) positive control groups were also included. In addition, this study used a somewhat more sensitive outcome measure for extravasation than albumin release as an indicator of increase in permeability of the blood-brain barrier, namely up-regulation of the water channel protein AQP-4 in the brain. After examination of brain tissue at the end of the study, no detectable up-regulation of AQP-4 was seen in the RF-exposed mice, while the chemical-injured positive control animals, as expected, showed substantial up-regulation.

Sirav and Seyhan (2011)[67] completed a similar study to their earlier investigation,[64] again in Wistar albino rats, and once again found that exposure to 900 or 1800 MHz RF fields for 20 minutes promoted a significant increase in albumin in the brains of male rats by comparison with sham-exposed animals. However, inexplicably no significant increase was seen in the RF-exposed female rats.

Table 7. Blood-brain barrier permeability and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Result	Comments
Salford et al. (2003)[60]	Fischer 344 rats	915 MHz CW and pulsed signal; SAR 2, 20, or 200 mW/kg or sham for 2 hrs	Albumin leaking into white and grey matter + "dark" or degenerating neurons in RF-exposed vs. control rats	Observations made 50 days post RF exposure
Finnie et al. (2006)[62]	Balb/c mice	900 MHz far field signal in utero; SAR 4 W/kg, or sham; 60 min/day, day 1–19 gestation	No albumin extravasation in RF-exposed or sham or cage control mice	
Finnie et al. (2006)[63]	Balb/c mice	900 MHz GSM pulsed far field signal; SAR 4 W/kg for 60 min/day for 7 days postnatally	No albumin extravasation in RF-exposed or sham or cage control mice	
Nittby et al. (2009)[61]	Fischer rats	900 MHz GSM signal from a mobile phone for 2 hours SAR of 0.0012, 0.012, or 0.12 W/kg or sham with 7 days recovery	Albumin positive foci around vessels in white and grey matter at 0.012 W/kg + dark neurons	Animals exposed in transverse electromagnetic transmission line (TEM) cell
Sirav and Seyhan (2009[64]	Wistar albino rats	900 MHz at 13.5 V/m or 1800 MHz at 12.6 V/m CW near field or sham exposure for 20 min	Increased extravasation of Evans blue dye in brain of male but not female exposed rats compared to sham	No SAR value given
Masuda et al. (2009)[52]	Fischer 344 rats	915 MHz pulsed at 16 or 217 Hz for 30 min, SAR of 0.02, 0.2 or 2.0 W/kg or sham- exposed in TEM cell	No increased extravasation of albumin in exposed rats	Cold- and chemical-control rats positive. Negative replication of Salford et al. (2003)[60]
McQuade et al. (2009)[65]	Fischer 344 rats	915 MHz CW and pulsed signal; SAR 0.002, 0.02, 0.2, 2.0 or 20 W/kg; or sham for 30 min	No significant increase in albumin extravasation in any RF- exposed vs. sham- or cage-control rats	RF exposure from protocol of Salford et al. (2003)[60]
Poulletier de Gannes et al. (2010)[51]	Fischer 344 rats	915 MHz GSM signal; SAR 0.14 or 2.0 W/kg for 2 hrs or sham	No increase in albumin extravasation in RF-exposed vs. sham- exposed and cage control rats. No dark neurons detected	Same basic protocol as Salford et al. (2003)[60]
Finnie et al. (2009[66]	Balb/c mice	900 MHz pulsed far field signal; SAR 4 W/kg or sham for 60 min/day, 5 days/wk, for 104 wks	No increase in AQP-4 expression in RF-exposed mice	
Sirav and Seyhan (2011)[67]	Wistar albino rats	900 MHz CW at 4.7 V/m, (SAR 4.26 mW/kg) or 1800 MHz CW (SAR 1.46 mW/kg) or sham for 20 min	Increased extravasation of Evans blue dye in brain of male- but not female-exposed rats compared to sham	

Summary

Recent studies have improved on the methods used in the mainly positive earlier studies[59,60] on blood-brain barrier permeability including improved procedures for tissue fixation, and albumin staining and more accurate and better described RF dosimetry.[68]

In addition, many of the recent studies[51,52,65,66] have incorporated positive control animals which are given brain injuries known to cause extravasation, and these studies have shown the expected extravasation in the injured animals but not in the RF-exposed ones. Overall, the weight of evidence for an adverse effect of RF-EMF on the integrity of the blood-brain barrier appears to have been considerably decreased based on results from most recent studies. A relatively recent review of the evidence on the effect of RF-EMF on blood-brain barrier permeability presented at a scientific meeting[69] concluded that such exposure had no adverse effect in the absence of significant tissue temperature increase.

6B.6.2 Brain physiology and behaviour and RF exposure (Table 8)

Concerns with the potential effects of RF exposure on physiologic processes within the brain have resulted in more than 30 studies since 2006. These include studies of changes in gene expression, apoptosis, and a variety of other potential effects.

Brillaud and colleagues (2007)[70] assessed the effects of acute exposure of 15 minutes to 900 MHz (SAR levels of 1.6 and 6.0 W/kg). The animals were killed at days 2, 3, and 10 post-exposure and brain tissue was examined. Results showed an increase in brain concentrations of glial fibrillary acidic protein (GFAP). GFAP is a protein expressed by astrocytic brain cells and is thought to be important in cell communication. However, the increase in GFAP levels was highest two days post-exposure, with a reduced level at three days, and none at 10 days, indicating that the GFAP increase was likely transitory.

A similar study by the same group, Ammari and colleagues, 2008,[71] examined the effect of pulsed 900 MHz GSM exposure on GFAP in Sprague-Dawley rats. The animals were exposed for 45 minutes per day at 1.5 W/kg or 15 minutes per day at 6 W/kg, five days per week, or sham exposed for 24 weeks. The rats were restrained during exposure for more precise RF dosimetry. Cage control animals were included in the study. Ten days after exposure was completed, the animals were sacrificed and brain tissue examined. At a SAR level of 6 W/kg, the exposure was associated with significant increases in levels of GFAP. It should be noted that this SAR level is much higher than seen with normal human RF exposure.

A further study by Ammari et al. (2010)[72] using a similar protocol to the study using Wistar rats, applied pulsed 900 MHz RF signal 45 minutes per day for eight weeks. Analysis of tissue from the several parts of the brain, namely the prefrontal cortex, cerebellar cortex and dendate gyrus at three and 10 days post-exposure indicated

elevated levels of GFAP, suggesting that the RF exposure was having a physiological effect, at least on astrocytic cells in the central nervous system.

Yilmaz et al. (2008)[73] found no brain changes after exposing Sprague-Dawley rats to 900 MHz GSM signal in speech mode for 20 minutes per day for one month. Similarly, Dasdag et al. (2009)[48] reported no significant changes in p53 activity in glial cells of Wistar rats after exposure to 900 MHz RF for two hours per day, seven days per week for 10 months, by comparison with that in sham-exposed rats.

Bas et al. (2009)[74] exposed Wistar rats to continuously modulated 900 MHz GSM signal (SAR 2.0 W/kg) or sham for one hour per day for 28 days and found a significant decrease in pyramidal cells in the brain of the exposed rats by comparison with sham- exposed animals. Pyramidal cells are thought to play an important role in cognitive functioning.

A study by Maskey et al. (2010)[75] showed loss of pyramidal cells in the hippocampus, a part of the brain involved in cognitive function, in mice after exposure to 835 MHz CDMA signal for a period of eight hours per day for three months at SAR levels of 1.6 W/kg.

Finnie et al. (2010)[76] examined acute and a long-term RF exposure to determine whether physiologic indicators of stress in the brains of mice could be evinced by exposure to pulsed 900 MHz GSM fields using a different measure of activity: microglial activation. Microglial cells are resident immune cells which are normally quiescent but in the presence of injury, toxic challenge or other stressors, are activated and become mobile. Mice were given a either a single whole-body exposure at SAR of 4.0 W/kg for 60 minutes or a series of such exposures on five successive days per week for 104 weeks. Other groups of mice were sham exposed. No increase in microglial activation detectable was seen in the short-term single 60-minute RF-exposed mice versus sham-exposed mice, or in the long-term two-year RF-exposed mice versus the sham-exposed comparison groups.

Table 8. Physiological changes in the brain and RF fields

Study	Animal Species/ Strain	Exposure	Results	Comments
Brillaud et al. (2007)[70]	Sprague-Dawley rats	900 MHz pulsed signal; SAR 6 W/kg; single 15 min exposure	Increased GFAP in RF-exposed rats compared to sham at 3 days, none at 10 days	
Ammari et al. (2008)[71]	Sprague-Dawley rats	900 MHz pulsed GSM signal; SAR 1.5 W/kg 15 min/day or SAR 6 W/kg or sham; 15 min/day 5 days/wk for 24 wks	Increased GFAP stained area in brains of rats exposed to 6 W/kg but not 1.5 W/kg	
Ammari et al. (2010)[72]	Sprague-Dawley rats	900 MHz pulsed GSM signal; SAR 1.5 W/kg or 6 W/kg or sham; 45 min/day, 5 days/wk, for 8 wks	Increased GFAP in rats exposed to RF at both SAR levels vs. sham	

Study	Animal Species/ Strain	Exposure	Results	Comments
Bas et al. (2009)[74]	Wistar albino rats	900 MHz modulated signal; SAR 2 W/kg (head) or sham; 1 hr/day for 28 days	Decrease number of pyramidal cells in cornu-ammonis area of brain in RF vs. sham rats	
Maskey et al. (2010)[75]	ICR mice	835 CDMA signal; SAR 1.6 W/kg 8 hrs/day for 3 mos or sham	Loss of pyramidal cells in RF-exposed animals compared to sham	
Dasdag et al. (2009)[48]	Wistar albino rats	900 MHz; SAR 0.17–0.58 W/kg (head) or sham; for 2 hrs/day, 7 days/wk for 10 mos	p53 not changed by RF exposure compared to sham-exposed rats	
Finnie et al. (2010)[76]	Mice; strain not named	900 MHz pulsed signal; SAR 4 W/kg; or sham for 60 min; or for 60 min 5 days/ wk for 104 wks	No increase in microglial activation in acute or long-term RF- exposed mice compared to sham mice	Positive control group showed substantial microglial activation

Summary

The results of a number of studies indicate that exposure to RF frequencies commonly used in mobile phone technology may produce some changes in the brains of both rats and mice. There are some concerns with the methodology of the positive studies; for instance, reported changes in GFAP levels at SAR levels of 6 W/kg raises the possibility that focal thermal changes rather than the RF exposure itself might have affected the outcome measure. These levels are much higher than humans are exposed to in day-to-day use of electronic devices. Moreover, some of the changes may be of short duration with reversion after cessation, at least for the effects of acute exposure. The relevance of these effects in animals and in humans is an open question, and more research will be needed to try to confirm the positive results and clarify their importance. In particular, long-term studies might be useful as most of the animal investigations carried out have been relatively short term.

6B.6.3 Behavioural studies and RF exposure (Table 9)

Several studies have been conducted using animal models to determine whether exposure to RF fields at low power levels can alter behaviour, disrupt learning, or affect cognitive function.

Lai (2004)[41] subjected three groups of rats to either an incoherent magnetic field alone, a 2450 MHz RF continuous field at a SAR of 1.2 W/kg, incoherent magnetic field (30–100 Hz field at 6 μT) + RF exposure, or sham exposure for one hour prior to each of six training sessions designed to teach the rats to locate a submerged escape platform in a water maze. One hour after the last training session, the platform was removed and the rats were subjected to a further test to assess the time spent swimming in the area the platform was previously located versus other areas of the water maze. Results showed that the group of rats exposed to RF only had a significant deficit in time spent in the previous platform location by comparison with sham-exposed animals. However,

the superimposition of the incoherent magnetic field on RF exposure appeared to attenuate somewhat the deficit seen in the rats exposed to 2450 MHz fields alone. No effect was seen in rats exposed to the incoherent field alone. The author concluded that exposure to the RF field may have induced temporary spatial learning and memory deficits but that the deficits could be attenuated by superimposition of the incoherent magnetic fields.

The findings from this investigation launched a series of studies to try to replicate an effect of RF fields on spatial learning. The initial studies by Cobb et al. (2004)[77] and Cosquer and colleagues (2005)[78] in rats using a water maze and 2450 MHz pulsed exposure with the same study protocols (although without the incoherent magnetic field exposure) found no difference between performance in the RF-exposed rats compared to the sham-exposed.

In a further study conducted by Kumlin et al. in 2007,[79] a group of 24 juvenile rats was exposed to a pulsed 900 MHz GSM signal for two hours each day, five days per week or sham beginning 24 days post-natal and continuing until age eight weeks. At the end of exposure, 18 of the RF- and sham-exposed rats were subjected to performance tests in a Morris water maze. The exposed rats showed significantly lower escape times than sham-exposed animals. The remaining six animals were sacrificed, and necropsy showed no effect on brain morphology, or blood-brain barrier permeability compared to the non-exposed rats.

Ammari et al. (2008)[80] subjected groups of rats to a pulsed 900 MHz GSM signal for 15 minutes per day at a high specific absorption rate (SAR 6.0 W/kg) or 45 minutes per day at a lower rate (SAR 1.5 W/kg) or sham for eight weeks or 24 weeks, and found no consistent differences between RF-exposed rats and sham-exposed rats in spatial memory. Cage control animals were found to have poorer performance in the test than either experimental group, but the authors attributed this to lack of daily handling, indicating that factors such as this need to be carefully controlled in future studies.

A further study by Narayanan et al. (2009)[81] was conducted by placing a mobile phone in vibratory mode at 900/1800 MHz GSM beneath the floor of a cage containing juvenile rats. Each day for four weeks the unrestrained rats were exposed to the fields associated with 50 missed calls with the phone in "vibrate" mode. At assessment of their spatial learning capabilities, the RF-exposed rats were found to take a longer time than control rats to locate an escape platform. However, the RF-exposure results may have also been confounded by the effects of the vibration of the phone on the rats. The study has also been criticized because the exposure protocol made it impossible to make realistic estimates of the actual RF exposure to the rats.

A Florida-based research group[82] conducted a study in which A□PPsw transgenic mice (which suffer from Alzheimer's-like cognitive symptoms) and their non-transgenic littermates were evaluated in a water maze, with initial results showing that the transgenic mice were, as expected, impaired compared to their non-transgenic

littermates. Beginning at five months of age, the mice were exposed to a 918 MHz GSM field at a SAR of 0.25 W/kg for two periods of one hour each day or sham exposure. After 6–7 months exposure to RF fields, transgenic mice showed significantly improved performance on most of the test measures compared to the sham-exposed transgenics. Some improvement was also seen in the RF-exposed non-transgenic mice compared to the sham-exposed littermates. However, the RF-exposed animals had a rectal temperature 1˚C higher than the non-exposed animals, which is high for the reported SAR of 0.25 W/kg, so it is possible that other factors in the exposure protocol may have affected the findings.

Table 9. Behavioural change and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Results	Comments
Lai (2004)[41]	Sprague-Dawley rats	2450 MHz CW signal; SAR 1.2 W/kg with or without 30–100 Hz magnetic field, 6 μT for 1 hr	Rats exposed to RF field had increased water maze escape time by comparison with sham	Increased escape time may indicate memory or learning deficits
Cobb et al. (2004)[77]	Sprague-Dawley rats	2450 MHz pulsed signal; SAR 0.6 W/kg or sham; 45 min/day for 10 days	No significant differences in water maze escape time or errors between RF-exposed and sham rats	
Cosquer et al. (2005)[78]	Sprague-Dawley rats	2450 MHz pulsed signal; 0.6 or 2 W/kg; 45 min/day for 10 days	No difference in water maze errors made by RF-exposed rats compared to sham-exposed	
Kumlin et al. (2007)[79]	Wistar rats	900 MHz GSM signal; SAR 3 W/kg; or sham; 2 hrs/day, 5 days/wk for 5 wks	Improved performance in water maze among RF-exposed rats compared to sham-exposed	Examination of brain tissue showed no morphology changes in RF-exposed rats
Ammari et al. (2008)[80]	Sprague-Dawley rats	900 MHz GSM signal; SAR 6 W/kg (brain) for 15 min or 1.5 W/kg for 45 min; 5 days/ wk for 8 or 24 wks	No consistent differences in spatial memory task between RF- exposed rats and non-exposed	
Narayan et al. (2009)[81]	Wistar rats	900–1800 MHz GSM phone signal; 50 missed calls per day for 4 wks or no exposure control	Spatial learning capacity of rats in RF-exposed groups compromised by comparison with control animals	No SAR given; phone on "vibrate" setting may have altered RF-rats response
Arendash et al. (2010)[82]	AβPPsw (transgenic) mice	918 MHz GSM signal; SAR 0.25 (whole body) 1 W/kg (brain); 1 hr/day from age 2 mos for 7 mos, or from age 5 mos for 8 mos	After 5–6 mos RF exposure transgenic rats showed improved water maze performance over their initial performance. No change in sham-exposed mice	RF exposure raised body temperature > 1˚C.

Summary

Like many of the other facets of RF exposure on animals, research on effects on behaviour and cognition are mixed, with several studies showing that RF exposure has an adverse effect, but most showing no effect or even improved performance. The

studies were, in general, fairly well conducted, using appropriate methods. Unfortunately, no variable such as RF frequency, duration of exposure, or period of life of the animal has emerged as being consistently associated with behavioural effects. However, much of the research in this field is still exploratory in nature, and it is difficult to judge the body of evidence to date. More studies are needed in this field of research.

6B.7 Somatic Systems and RF Exposure

6B.7.1 Immune function and RF exposure (Table 10)

Several studies of immune function in the presence of RF fields have been conducted since 2005.

Nasta et al. (2006)[83] examined the effect of RF exposure on a number of immunologic parameters in C57BL/6 mice including frequency of several types of B and T cells important in immune function and production of antibodies in the spleen. Groups of mice separated within polycarbonate containers were exposed to 900 MHz GSM signal in a TEM cell at a SAR of 2 W/kg. RF exposure or sham continued for two hours per day, five days per week for four consecutive weeks. A jacket containing circulating water was positioned under the floor of the exposure set-up to keep temperatures stable during RF exposure and ensure against thermal effects. Results showed that the frequency of differentiating transitional 1 and 2B (T1, T2) cells, or mature follicular B and marginal zone B cells in the spleen were unaffected by exposure to RF fields in comparison with sham-exposed mice. An in vitro antibody production test was conducted on spleen cells from non-immunized RF field-exposed and sham-exposed mice. Antibody production by spleen cells was unaffected by RF exposure. The authors concluded that the study offered no support for the theory that RF exposure may alter B-cell peripheral compartment and antibody production.

Prisco and colleagues (2008)[84] examined the ability of cells from C57BL/6 mice exposed to RF fields by comparison with those from sham-exposed animals to repopulate marrow in mice exposed to marrow-lethal X-irradiation. The mice were exposed in a TEM cell to 900 MHz GSM modulated signal or sham for two hours per day, five days per week for four weeks. After exposure, bone marrow cells from the RF-exposed and sham mice were injected into X-irradiated mice. At three weeks and six weeks post-exposure, transplanted mice were killed and immune components were examined. Results showed no differences between cell populations in the marrow of mice transplanted with marrow from RF-exposed and sham-exposed mice, or in production of interferon γ, a cytokine produced by natural killer and natural killer T-cells critical in immune modulation.

Perhaps the most important recent studies in immune function relating to RF field exposure are two investigations conducted in France and Russia to replicate early reports in Soviet journals[85,86] suggesting adverse effects on the immune systems of rats

resulting from chronic 2375 MHz RF exposure at electric field levels of 5 W/m^2. Although SAR levels were not presented in the original series of papers, this power density would be associated with values of about 0.6 W/kg. The Soviet studies indicated RF exposure disrupted the antigenic structure in rat brain cells. The exposure also produced modification in the number of plasmocytes in the spleen and the number of small lymphocytes in the marrow, perhaps due to an autoimmune reaction in the animals. Further, the studies showed that intraperitoneal injection of serum from chronically RF-exposed animals into non-exposed pregnant rats resulted in increased fetal mortality and decreased weight in their offspring compared to that seen in pregnant rats receiving non-RF-exposed rat serum injection. French[87] and Russian[88] scientists launched independent studies (but with a common protocol) to try to confirm or refute the Soviet results.

The Russian study (2010)[88] exposed Wistar rats to 2450 MHz continuous wave RF far field (whole body SAR 0.16 W/kg) or sham in an anechoic chamber for seven hours per day, five days per week for a period of 30 days. At seven days post-exposure, some of the animals were sacrificed and examination using complement fixation tests showed minor increases in antibody production in the brain (but not in liver) tissue extract in the RF-exposed rats compared to sham rats. In addition, at seven and 14 days post-exposure, serum taken from exposed and sham rats was injected intraperitoneally into pregnant rats. Among the pregnant rats injected with serum from the RF-exposed rats, embryo mortality at day 20 of pregnancy was higher by comparison with that seen in the dams injected with serum from the sham-exposed rats. Postnatal offspring mortality comparing pregnant cage control rats with sham and RF-injected pregnant rats was planned in the study but was hampered by unaccountably high mortality (34%) among rats in the cage control group. No comparisons of offspring mortality among RF, sham and cage control rats were therefore presented in the paper, presumably because the unknown factors leading to the high mortality among cage control animals might conceivably have affected the RF- and sham-exposed rat groups.

The French study (2009)[87] followed the same protocol as the Russian study.[88] The French group did not repeat the complement fixation tests of the Russian group for antibodies in brain tissue because the differences between the RF- and sham-exposed groups were regarded as not important. They used ELISA tests (which use optical density to quantitatively assess antibody prevalence) exclusively to test for production of antibodies to brain and liver tissue. Sixteen antigens were used to test against IgA, IgM and IgG immune globulins and analysis of the ELISA data showed no significant differences in antibody production in brain and liver tissue samples between cage control, sham or RF-exposed rats. Among the pregnant rats injected intraperitoneally with serum taken at days 7 and 14 post-exposure from RF-exposed, sham-exposed and cage control rats, no significant differences were seen in the number of live and dead fetuses during pregnancy, or number of pups, sex ratio, mean body weight, viability or physical development to age 28 days. The authors concluded that the results did not support the original Soviet findings.

Due to the differences in the results of the two studies, the WHO EMF Project convened an international oversight committee[89] to review the results of the two studies. They determined that the more subjective aspects of interpreting the complement fixation tests to determine antibody levels in the Russian study rendered those results questionable, particularly when an error analysis carried out by the international oversight committee determined that the differences seen between the RF- and sham-exposed tests would have been expected due to normal variation when employing this methodology. The significant differences in intrauterine fetal mortality between rat dams injected with RF- and sham-exposed serum in the Russian study was felt to be questionable due to the extraordinarily high mortality among the cage control (and the RF- and sham-exposed) pups postnatally, suggesting that factors other than those under study were likely to have influenced study prenatal results.

Table 10. Immune function and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Result	Comments
Nasta et al. (2006)[83]	C57BL/6 mice	900 MHz GSM modulated signal; SAR 2 W/kg or sham for 2 hrs/day, 5 days/wk for 4 wks	No changes in B-cell peripheral differentiation or antibody production from RF exposure	
Prisco et al. (2008)[84]	C57BL/6 mice	900 MHz GSM modulated signal; SAR \2 W/kg, 2 hrs/day, 5 days/wk, for 4 wks	No effect from RF exposure on spleen B or T cell percentages proliferation rates or γ IFN production in transplanted mice	RF-exposed cells transplanted into mice which have undergone marrow-lethal x-rays
Poulletier de Gannes et al. (2009)[87]	Wistar rats	2450 MHz CW signal; SAR 0.16 W/kg or sham for 7 hrs/day, 5 days/wk for 30 days	No differences in antibody levels in RF- exposed vs. sham-exposed rats; no differences in embryo mortality in dams injected with RF- exposed vs. sham-exposed serum	
Grigoriev et al. (2010)[88]	Wistar rats	2450 MHz CW signal; SAR 0.16 W/kg (whole body) or sham; 7 hrs/day, 5 days/wk, for 30 days	Higher antibody levels in RF-exposed mice brain but not liver; embryo mortality higher in dams injected with RF-exposed serum than sham serum	Unaccountably high mortality in cage control dams prevented comparison of offspring immune characteristics

Summary

The major concern from early Soviet studies that RF-EMF fields could affect the immune system of animals, and that the increased risk for adverse effects could be transmitted to offspring through serum injection, has not been confirmed by the well-conducted French study. The WHO international oversight committee which examined the results of both the Poulletier de Gannes et al. (2009)[87] and Grigoriev et al. (2010)[88] studies concluded that the weight of evidence from both studies taken together indicated that

intraperitoneal injection of serum from rats exposed to RF exposure is unlikely to influence development and mortality among fetuses of pregnant rats and unlikely to affect pup mortality postnatally. The number of animals used in each study (48 each) was relatively small and even though the results of the two studies indicated the absence of effects due to RF exposure, they lacked the power to be definitive. The Russian authors continue to maintain that their results support at least some of the earlier Soviet observations.[90] The committee recommended against repeating the studies, as this was not apt to increase knowledge in this field. Instead they recommended that investigators should, in future, pursue possible immune effects of RF fields in children if they prove more susceptible to RF-related adverse immune effects. Unfortunately, the same caveats noted earlier to reaching definitive conclusions about other adverse health effects of RF fields also apply to immune effects—namely that the RF frequency, duration of exposure, possible biologic mechanism, and outcome measures of primary importance remain unknown.

6B.7.2 Endocrine function and RF exposure (Table 11)

Most of the focus in animal studies of endocrine function has been on investigations of the influence of RF exposure on melatonin synthesis. Bakos and others (2003)[91] exposed adult male Wistar rats to a 900 MHz-modulated GSM signal at SAR values of 0.009–0.012 W/kg or sham, or 1800 MHz-modulated GSM signal at SARs of 0.02–0.45 W/kg or sham. The exposure was conducted in a TEM cell with animals exposed for two hours between 8:00 am and 10:00 am on even days and 10:00 am to noon on odd days daily for 14 days. Urine was collected from the animals from 12:00 am to 8:00 am and analysed for melatonin secretion. No significant differences were seen in rats with either 900 MHz or 1800 MHz RF field exposure compared with sham-exposed rats.

Koyu and colleagues (2005)[92] also conducted a study to determine the effects of RF exposure on melatonin secretion. Sprague-Dawley rats were exposed to either 900 MHz GSM or 1800 MHz signal at SAR levels of 2 W/kg or sham for 30 minutes per day, five days per week for four weeks. Melatonin was measured in serum using radioimmune assay, and no significant differences in levels were seen in rats exposed to either 900 or 1800 MHz fields by comparison with sham-exposed rats.

Hata et al. (2005)[93] examined the effect of a 1439 MHz TDMA signal at 2 W/kg whole body (7.5 W/kg head) on melatonin production in Sprague-Dawley rats. Animals were exposed for four hours on day 1 during a “dark” period in the lab to either 1439 MHz RF or sham. Cage control and light control animals were also included in the protocol. Blood and pineal glands were removed and melatonin and serotonin concentrations assessed. Results showed no differences in melatonin or serotonin levels in the RF-exposed rats compared to sham-exposed rats.

Lerchl and colleagues (2008)[94] exposed hamsters for 24 hours per day for 60 days to RF fields at 383 MHz, 900 MHz and 1800 MHz at whole body SARs of 0.08 W/kg or sham. Melatonin concentrations in sera and from pineal gland homogenates collected

from the animals at the end of the study showed no significant differences between RF-exposed animals at any of the three wavelengths and the sham-exposed controls.

Table 11. Endocrine function and RF field exposure in animal models

Study	Animal Species/ Strain	Exposure	Result	Comments
Bakos et al. (2003)[91]	Wistar rats	900 MHz signal; SAR 0.009–0.012 W/kg or 1800 MHz GSM signal; SAR 0.02–0.045 W/kg or sham; 2 hrs/day (at 08:00 or at 10:00) for 14 days	No significant effect on melatonin secretion in RF-exposed vs. sham-exposed rats	
Koyu et al. (2005)[92]	Sprague-Dawley rats	900 or 1800 MHz CW signal SAR 2 W/kg (max) or sham; 30 min/day, 5 days/wk for 4 wks	No significant effect on melatonin secretion from RF exposure	Time of exposure not given in the study
Hata et al. (2005)[93]	Sprague-Dawley rats	1439 MHz TDMA signal SAR 2 W/kg (7.5 W/kg head) for 4 hrs	No significant effect from RF exposure on melatonin	
Lerchl et al. (2008)[94]	Djugarian hamster	900 or 1800 MHz GSM or 383 MHz signal; SAR 0.08 W/kg, 24 hrs/day for 60 days	No effect of RF exposure on melatonin	

Summary

Studies of melatonin levels in animals have been negative, and the data provide no support for the possibility that RF exposure can decrease melatonin levels.

6B.7.3 Testicular function

Because of concern among the general public that exposure to RF electromagnetic fields might affect reproductive capacity, a number of studies on semen analysis have been conducted. These are summarized along with mechanistic studies and human investigations in Section 10 of the report.

6B.7.4 Female reproductive function and RF exposure (Table 12)

In Korea, Lee and colleagues (2009)[95] evaluated the effect of exposure to 3G code division multiple access (CDMA) and wideband code division multiple access (WCDMA) RF signals at SAR levels of 2 W/kg in ICR mice. Groups of pregnant dams (and their fetuses) were exposed to either 848.5 MHz CDMA or 1950 MHz WCDMA signal or both simultaneously for two sessions of 45 minutes each for days 1–17 of gestation. On day 18, all dams were humanely killed and examined for numbers of viable fetuses, number of dead fetuses, fetal weights, and a number of other measures. In addition, fetuses were examined for gross physical malformations, weight, body length, and skeletal malformations. No differences were seen in any of the outcome measures between the RF-exposed dams and sham-exposed dams. No differences in malformations, weight, length or other characteristics were seen in RF-exposed fetuses compared to sham-exposed fetuses.

Similar negative results were seen in a study of pregnancy outcome and visceral and skeletal abnormalities among offspring in pregnant Sprague-Dawley rats exposed to 1900 MHz WCDMA for 90 minutes per day on days 7–17 of gestation[96] and in pregnant C57BL mice (and fetuses) exposed to 1766 MHz UMTS signal or sham 24 hours per day in a series of studies involving four mouse generations.[97]

Investigators in Japan[98] exposed pregnant Sprague-Dawley rats to 2140 MHz WCDMA downlink signals in a search for adverse pregnancy outcomes, including visceral and skeletal abnormalities in offspring. Pregnant rats were exposed at two different relatively low SAR levels (0.028–0.040 W/kg or 0.066–0.093 W/kg) for 20 hours per day from gestational day 7 to postnatal day 21. No abnormalities were seen in the RF-exposed first generation (F1) offspring. After weaning, F1 offspring were removed from the exposure boxes, and at 10 weeks of age randomly selected males and females were isolated for breeding. After mating, pregnant dams were sacrificed at gestational day 20 and all F2 fetuses removed and examined for abnormalities. No abnormalities in fertility and embryo loss were seen in the RF-exposed F1 dams, and no visceral or skeletal abnormalities were found in their F2 offspring attributable to RF exposure.

Sambucci et al. (2010)[99] examined pregnancy outcome and immunologic function in C57 BL/6 mice after exposure while restrained to a 2450 MHz pulsed Wi-Fi signal at a SAR level of 4 W/kg or sham two hours per day from gestational day 5 through 19. No significant effects were seen on spleen cell number, B-cell frequency or antibody serum levels in the RF-exposed dams compared with sham-exposed animals. In the offspring, assessed at five and at 26 weeks of age, no immunologic effects were seen in in utero RF- exposed offspring compared to those not exposed.

Fragopoulou and colleagues (2010)[100] in Greece completed a study using BALB/c mice exposed in utero to 900 MHz GSM RF fields at SAR levels of 0.60–0.94 W/kg for six or 30 minutes per day from gestational days 0–21 and found an initial delay in ossification of cranial bones in RF-exposed pups compared to sham-exposed animals. However, this difference disappeared by day 35 after birth. An actual phone may have been used to provide RF exposure, casting some doubt on the RF dosimetry.

A number of other investigations not shown in Table 12[101-103] likewise found no effects of RF exposure.

Table 12. Female reproductive function and RF field exposure in animal models (2009–2011)

Study	Animal Species/ Strain	Exposure	Results	Comments
Lee et al. (2009)[95]	Pregnant ICR mice and their offspring	848.5 MHz CDMA (SAR 2.0 W/kg) and/or 1950 MHz WCDMA signal; SAR 2.0 W/kg in utero or sham for 2 sessions of 45 min each for days 1–17 of gestation	No adverse effects seen in offspring exposed to CDMA, WCDMA or both signals	Lack of thermal effects confirmed by rectal temperature before and after RF
Ogawa et al. (2009)[96]	Pregnant Sprague-Dawley rats	1900 MHz WCDMA signal SAR 0.67 or 2 W/kg to mother or sham; 90 min/ day on days 7–17 gestation	No effects seen in mothers or offspring	
Sommer et al. (2009)[97]	C57BL mice	1966 MHz UMTS 24 hrs/day lifelong; SAR 0.08, 0.4, 1.3 W/kg, or sham; as each set of pups is weaned, parental animals sacrificed; experiment continues over 4 generations	No effects on fertility, number and develop-ment of pups attributable to RF	
Takahashi (2010)[98]	Sprague-Dawley rats	2140 MHz downlink WCDMA signal 20 hrs/day from gestational day 7 through postnatal day 21; SAR dams 0.028–0.040 W/kg, or 0.066–0.093 W/kg); SAR fetuses 0.061–0.067 W/kg or 0.143–0.156 W/kg or sham	No adverse results in F1 dams or their offspring due to exposure to RF	
Sambucci et al. (2010)[99]	C57BL/6 mice	2450 MHz pulsed signal; SAR 4 W/kg or sham; 2 hrs/ day from gestation days 5–19	No significant effects on immunologic functions in mouse offspring	Animals restrained for accurate dosimetry to fetuses
Fragopoulou et al. (2010)[100]	Pregnant BALB/c mice	900 MHz signal from mobile phone in talk mode; SAR 0.6–0.94 W/kg, or sham; 6 or 30 min/day from gestational days 0–21	Initial delay in ossification in cranial bones of offspring; no effects by day 35	Actual mobile phone may have been used for exposure

Summary

Studies in female animals examining the putative adverse effects of RF fields on litter size, aspects of the health of offspring, prevalence of congenital abnormalities at birth and other endpoints have been almost uniformly negative, and there seems little probability, in animals at least, of adverse effects from in utero exposure to RF fields.

6B.7.5 Longevity and RF exposure

Although none of the two-year cancer bioassays have found differences in longevity between RF-exposed and non-exposed animals, two interesting studies in rats have recently been completed (data not tabulated). Adang et al. (2009)[104] in Belgium exposed four-month-old Wistar albino rats to 970 MHz pulsed or continuous wave or sham RF exposure two hours per day, seven days per week during a 21-month period.

After 14 and 18 months exposure, the white blood cell count in the continuous wave exposed rats was elevated by comparison with the sham-exposed group. After 24 months, mortality in the animals in both the pulsed and continuous wave-exposed groups appeared to be somewhat higher than that in the sham-exposed group although the results were not statistically significant.

Bartsch and colleagues (2010)[14] conducted a series of four experiments with female Sprague-Dawley rats. In the first two experiments, the rats were exposed to 900 MHz signal pulsed at 217 Hz or to sham exposure, starting at 52–70 days after birth and continuing until they were 580 or 770 days old; in neither experiment did any adverse effects materialize in the RF-exposed group by comparison with the sham-exposed group. In experiments 3 and 4, RF exposure was maintained even longer in the animals' lives. In experiment three, after 799 days, median survival was lower in the RF exposed group, and a similar finding was seen in the rats in experiment four after 852 days by comparison with the sham group. The authors noted that month of birth is known to influence lifespan in these animals and so results should be interpreted with caution; as well, seasonal influences in diet may contribute to discrepancies in lifespan among rats, although no information is presented in the paper on these factors.

Summary

The results of the two studies, while quite "soft," suggest that more attention needs to be paid to very long-term effects of RF-EMF. Although it is impossible to suggest a biologic mechanism which might explain the findings, results of both studies described above suggest that lifelong exposure to RF fields may shorten lifespan, perhaps in conjunction with other factors, at least in animals. As noted, several issues cloud the findings, and variables such as animal strain and environmental conditions under which animals are kept may be important, as well as diet. Studies commissioned as part of the US National Toxicology Program's cellular phone RF series, and currently underway, should be able to more closely monitor a variety of factors which affect animal lifespan while evaluating the independent effect of RF. Reports on these studies are to be available in 2014. A brief fact sheet is accessible at:

http://www.niehs.nih.gov/about/assets/docs/cell_phone_fact_sheet.pdf

6B.8 Discussion

Overall, studies in animals have not provided convincing evidence of major adverse effects from exposure to RF-EMF fields. Many new studies have been undertaken and completed since 2005, with improvements in study design and in execution by comparison with earlier efforts. Findings from most studies for a variety of biologic effects have been negative.

Investigations of the carcinogenicity of RF field exposure in animals have been virtually uniformly negative, and even studies of RF-EMF as a promoter in conjunction with known

carcinogens offer little evidence of adverse effect. Studies conducted with animals known to be at high risk of CNS, mammary, and other cancers have also been negative.

Studies of genotoxic effects, gene expression and apoptosis have yielded inconsistent results. One of the difficulties in going forward is that no specific frequency, timing or duration of exposure appears to distinguish positive studies from negative ones.

Investigations of putative effects of RF fields on the brain and central nervous system have found no consistent evidence of effect at the field strengths to which human beings are exposed to on a day-to-day basis. There was some indication of transitory increases in specific brain proteins and loss of pyramidal cells; however, further evaluation of these findings is needed in future studies. Most recent investigations of blood-brain barrier leakage have not found an increase in permeability due to exposure to RF-EMF. The newer studies have controlled more carefully for thermal effects which are known to alter blood-brain barrier permeability. They have incorporated improvements in methods for fixating brain specimens and techniques for visualizing changes in neural tissue. The addition of positive control groups as well as cage and sham controls have also provided useful comparison measures. Concern about increased blood-brain barrier permeability due to RF fields has been substantially reduced by results of recent investigations.

Behavioural studies aimed at evaluating adverse or beneficial effects of RF-EMF on spatial memory in animals have been mixed to date, with most studies showing no overall differences between RF- and sham-exposed animals; but other areas of brain function have yet to be thoroughly studied.

Recent reports on attempts to confirm early Soviet reports of adverse immune effects in rat embryos and in rat pups exposed in utero to 2450 MHz RF fields[87] were completely negative. The Russian[88] study did produce results indicating some support for the suggestion in early Soviet studies that injection of serum taken from animals exposed for 30 days to 2450 MHz fields and injected into pregnant rats might cause adverse effects in their embryos during gestation. However, problems with excess mortality in the RF- and sham-exposed animals and particularly in cage control rats cast doubt on any positive findings from the Russian study. After examination of the French and Russian protocols and results by an international oversight committee appointed by the World Health Organization,[90] the positive results seen in the Russian studies were effectively discounted. No other aspects of immune function in animals have been shown to be influenced by RF exposure in recent studies.

The results of studies of the effect of RF-EMF on pregnancy and reproductive function in female animals have been overwhelmingly negative.

To date, relatively little attention has been paid to the issue of whether young animals are more susceptible to adverse effects due to RF field exposure than older animals. A recent review of the relatively scant evidence generated from studies designed to address other issues has suggested that there is no strong support for vulnerability of

young animals to RF.[105] However, as immune function in many animals is immature at birth, the international oversight group, which reviewed studies presented by French and Russian scientists, specifically recommended further investigations in young animals exposed to RF fields by comparison to sham-exposed animals.

While the results of animal studies to date do not provide evidence for any strong or consistent biologic effects from exposure to RF fields, some caution is in order. Most positive results in animal studies have not been replicated in subsequent investigations, in part due to the wide variety of exposure methods, animal strains, and RF signal characteristics employed by investigators. Closer comparability of protocols, animal strains, and RF dosimetry employed in studies is not likely to take place in the immediate future as it is not known what frequency ranges, characteristics (pulsed or continuous wave) and duration and intensity of exposure are most important for effects to occur. Furthermore, no specific animal model or period of life has been identified as being most useful in studies of RF exposure. Perhaps the most important problem for future research in this area is the lack of a plausible mechanism by which RF exposure might cause adverse biological effects. Such a mechanism would surely sharpen the focus of future research.

A large series of studies on the effects of RF exposure in animal models is currently being sponsored by the National Toxicology Program within the National Institute for Environmental Health Services in the US. Reports on these studies, expected in 2014, may provide more definitive information.

6B.8.1 Research limitations and gaps in the literature

Several research limitations were apparent in the reviewed studies. There is a need for:

- Consistent use of a uniform set of criteria for describing RF exposure in animal studies and a possible model for such criteria
- Consistent use of good restraint methods designed to minimize animals' stress and thermal effects during exposure. Restraints will also improve the precision of field application where organ-specific exposure is required by a research protocol
- Consistent use of good containment vessels such as reverberation chambers for ensuring uniform RF fields for animals undergoing RF exposure in experiments where restraints are inappropriate.
- Research gaps include the need for:
    - Better more sensitive methods and more quantitative models for investigation of potential effects of RF exposure on animal behaviour
    - Studies of the very long-term effect of RF exposure with follow-up to the end of animals' natural life where this is economically feasible
    - Direct comparison studies of RF effects in young vs. adult animals of the same strain for a variety of potential biologic outcomes.

6B.9 References

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Section 7

The Use of Electromagnetic Fields in Medicine and Its Effect on Patients and Health Care Workers

Table of Contents

Summary

- This section of the toolkit presents studies on the exposure and health of patients and health care workers exposed to RF from medical devices.
- Electromagnetic fields (EMF) of lower frequencies up to 200 MHz are commonly used in medicine for diagnosis and therapy; included are exposures to radiofrequency (RF) fields above 100 kHz (0.1 MHz).
- Three main EMF applications in medicine are magnetic resonance imaging (MRI), radiofrequency ablation (RFA) used in cardiology and tumour therapy, and localized dielectric heating (short wave diathermy) used in physiotherapy.
- MRI produces three different fields to generate images: (1) a static magnetic field of zero frequency; (2) low power time-varying magnetic field gradients (100 Hz to 1 kHz); and (3) RF fields (10 to 400 MHz). No long-term effects of EMF exposures to MRI patients on reproductive, cardiovascular and cognitive function outcomes have been reported. While MRI operators may be exposed to RF when working less than 0.5 meters from the bore, there is no indication of chronic effects from their occupational exposure to the EMF fields.
- RF ablation is a minimally invasive medical procedure that destroys tumours and unhealthy tissue in heart muscle by thermal means from RF. Complications to patients, which may arise due to non-target thermal damage, are usually reversible. We found no studies of occupational health risks for workers administering RF ablation.
- Diathermy is used in physiotherapy to heat surface or deep tissue to relieve joint and muscular problems. There was no literature concerning adverse effects on patients. Although female physiotherapists have been found to be at a slight increased risk for spontaneous abortions and heart disease, these may be relevant only to the older practice of microwave diathermy rather than the more current common use of shortwave diathermy.

7.1 Introduction

EMF of lower frequencies up to 200 MHz is commonly used in medicine for diagnosis and therapy. EMF is classified according to frequency and type of field. Static magnetic fields do not vary in time, while time-varying EMF up to 100 kHz is classified as low frequency (LF) fields. Above 100 kHz and up to 300 GHz, it is referred to as RF fields.

Patients are exposed to EMF from specific medical devices when undergoing diagnosis and/or therapy. Attending personnel (medical, paramedical) also may be exposed to RF in the course of their work.

The purpose of Section 7 of the toolkit is to review available information related to exposure to RF from medical devices and possible health effects on patients and health care workers.

7.2 Methods

A literature search for peer-reviewed publications and reports relating to exposure and adverse health effects of EMF in medicine was carried out using EBSCO and OVID databases. The key words used in this search were "magnetic resonance" or "magnetic resonance imaging" or MRI or "radiation ablation" or "radiofrequency ablation" or "radio frequency ablation" or "diathermy" combined with "health effect" or "health outcome" or cancer and occupation* or complication or "physical therapist" or physiotherapist or staff or worker or personnel or technician or patient. Additional searches were done manually from the reference lists and by using Google.

Because few review articles and primary reports had been published on long-term health effects of exposure to EMF on patients or health care workers, none of the English publications were initially excluded.

7.3 EMF Applications in Medicine

A combination of magnetic and RF fields are employed in diagnostic imaging. Applications involving heat-generating RF waves are used for therapeutic purposes.

The three main EMF applications and areas of medicine using EMF sources are:

- MRI – diagnostic imaging
- RF ablation – cardiology and cancer (tumour) therapy
- Localized dielectric heating (shortwave diathermy) – physiotherapy.

Table 1 below summarizes power and frequency ranges applicable to various medical devices: MRI; cardiology; physiotherapy; and tumour therapy.

Table 1. Frequency and power of EMF machines used in medicine

Application		Power or Magnetic Field Strength	Frequency
MRI	Main magnetic field	1.5, 3 Tesla (T)	64, 128 MHz
	Gradient magnetic field	few milliTesla (mT)	Multi-frequency in the MHz range
	Radiofrequency field	Up to few kilowatts but not radiative (no radio waves emitted)	100 to 200 MHz
Cardiology		RF generator: 50 Watts	460–480 KHz
Tumour Therapy		RF generator: 200 Watts	461 KHz
Physiotherapy		RF generator: 500 Watts	27.12 MHz

7.3.1 Magnetic resonance imaging

MRI is a medical imaging technique used in radiology to visualize internal structures. An MRI unit produces three different EMF fields to generate images:

- A static magnetic field of zero frequency (average magnetic flux density of 1.5-3 Tesla) produced by a large magnet for the alignment of hydrogen nuclei (protons) inside the body
- Low power time-varying magnetic field gradients (100 Hz-1 kHz) generated by small magnets in three orthogonal planes (X, Y and Z directions) to provide the spatial position of the protons. Further, these MF gradients allow image slices to be created by focusing on the patient body part under examination
- RF fields (100-200 MHz) produced in the non-radiative near field of the emitter to excite the protons (in the body) and cause the protons to emit radio waves (radiative RF) for the acquisition of anatomical images.

The layout of a typical MRI unit is given in Figure 1 below[1] showing "controlled" areas and "inner controlled" areas. The maximum level of the static magnetic fields in the controlled area is kept under 0.5 milliTesla (mT). For the inner controlled area in the immediate vicinity of the imaging equipment, the limit of the static magnetic field is set at 3 mT (30 Gauss). RF shielding surrounding the MRI is placed to prevent exterior RF interferences from affecting the operation of the imaging unit.

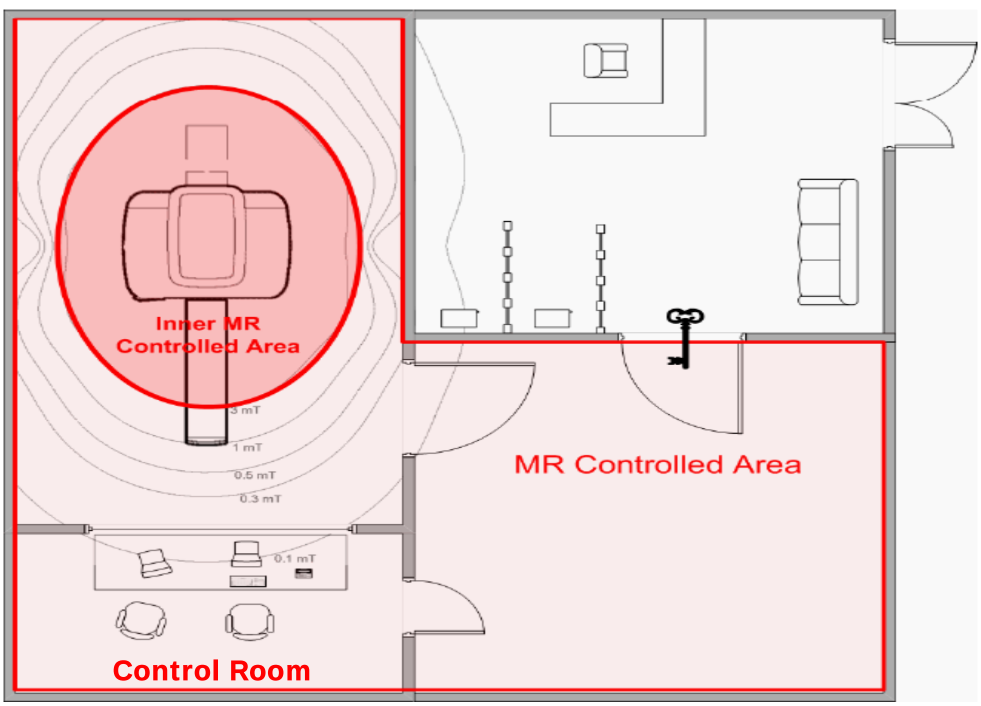

Figure 1. Example of MRI Layout[1]

As a source of non-ionizing radiation, MRI is considered safer than x-ray imaging and, as such, represents an alternative to some x-ray diagnostic procedures, particularly for imaging children and pregnant patients. MRI is best suited for imaging soft tissue, making it particularly useful to image some principal anatomical structures (e.g., brain, muscles, heart) and to detect cancers.[2,3] Each year, approximately 60 million MRI scans are performed worldwide.[4]

7.3.1.1 Adverse health effects for patients exposed to MRI fields

The RF frequencies used in an MRI scanner can result in high absorption of RF over the whole body, with the eyes and testes being especially vulnerable to heating effects. Metal-based pigments such as tattoos increase the probability of burns, as do metallic implants. However, there have been no epidemiological studies on long-term health effects specifically attributed to RF fields associated with MRI procedures.[5] Rather, adverse outcomes for patients who have undergone MRI treatments have been associated with their exposure to static magnetic fields.

Cancer: Although there is no epidemiological literature on cancer attributed to patients being examined by MRI, there is suggestive evidence of possible DNA damage as micronuclei induction (associated with carcinogenesis) has been shown to temporarily increase during MRI diagnostic scans.[5]

Reproductive and development outcomes: The available data on fetal exposure to EMF during MRI examinations do not point to adverse effects on the developing fetus.[6] The main concern would be the temperature increase that could be generated by the RF fields of MRI. However, temperature increases in the fetus during MRI examinations are under strict guidelines and unlikely to reach 0.5°C. A 2008 UK-HPA review[7] of studies related to reproductive and development outcomes concluded that there was no evidence of adverse effects on eye and ear functions or reproductive outcomes on children previously exposed to MRI in utero.

Cardiovascular effects: During MRI examinations, the time-varying magnetic field gradients at frequencies ranging from 10 to 100 Hz could cause cardiac problems to patients if the induced current density is higher than the cardiac stimulation threshold of 1.2 Ampere/m^2.[1] However, modern MRI machines are designed to deliver lower time-varying fields, far below the cardiac stimulation threshold current density.[8,9] Furthermore, no significant cardiovascular changes in patients undergoing MRI procedures have been reported.[10] A consideration is that above 100 Hz, muscle tissue (including cardiac muscle) is less responsive to electrical stimulation.

Peripheral nerve stimulation: Time-varying magnetic fields up to 5 kHz can induce currents in the MRI patient. Peripheral nerve stimulation is possible but only when the magnitude of the induced current densities is sufficiently high. The threshold current density for nerve stimulation is comparable to the level for cardiac stimulation, but MRI machines are designed to operate far below this threshold by keeping the current

densities below 0.4 Ampere/m^2.[8] At frequencies higher than 5 kHz, nerve cells are less responsive to electrical stimulation.

Effects on cognitive function: A recent study by Schlamann et al. involved the participation of 25 volunteers without history of neurological diseases in a series of neuropsychological tests before and after undergoing MRI examinations at 1.5 Tesla and **7** Tesla.[11] The testing, which focused on the volunteers' attention capabilities, consisted of paper-based and computer-based neurobehaviorial tests. The study did not reveal any adverse effects on cognitive test performance after exposure to MRI fields.

Non- specific symptoms: Acute symptoms such as vertigo and nausea may be due to low frequency sensory effects which can occur with rapid patient movement inside the MRI machine. However, these symptoms are less frequent when patients are carefully moved at a slow pace into the magnet bore and are not associated with any long-term consequences. Such non-specific symptoms may also result from anxiety due to the claustrophobic nature of the procedure.

Some precautionary measures to protect patients from any potential harmful thermal effects are recommended when undertaking MRI procedures.[12] For vulnerable patients, including cardiac patients, those wearing metallic implants, pregnant patients and children, there are general guidelines to limit increase in the core temperature of the patients undergoing MRI procedures.[12,13] In general, whole body temperature increase to the patient should be less than 0.5°C; temperature for the head region should be less than 38°C; temperatures for the trunk less than 39°C; and for extremities, temperatures should be less than 40°C. The fetus is particularly vulnerable to RF exposures; exposures within allowable limits to the pregnant mother's abdomen may result in excess RF absorbed by the fetus.[14]

7.3.1.2 Occupational health risks related to MRI

In general, health care workers in MRI are only exposed to the static magnetic field because the time-varying magnetic field gradients and the RF fields are essentially only present inside the scanner. However, incident field limits of RF can be exceeded within short distances (0.2–0.5 m depending on the model) of the bore entrance during the scan acquisition (estimated to occur during 3% of scans or 40,000 examinations a year in the UK).[4] This is an issue particularly with open scanners and possibly the new generation of wide bore scanners.

Patients are exposed to static magnetic fields (zero Hz frequency) up to 3 Tesla during the MRI examinations while health care workers are regularly exposed to much lower fields ranging from .5 mT to 3 mT (mT being one thousandth of a Tesla). Occupational exposures from medical RF devices differ from patient exposures in that they occur for longer periods during the day and over the duration of employment; however, the intensity of exposure may be minimal.

Workers exposed to EMF in the manufacture of MRI scanners had more vertigo, metallic taste, headache and concentration problems than workers in a reference department but these symptoms were transient, disappearing after exposure ended.[15] Field surveys also revealed that MRI engineers and nurses had the following symptoms: nausea, concentration problems, memory loss, tiredness or drowsiness, illusions of movement and ringing sensation in the head during their work, and sleep disorders. The frequencies of these symptoms were mainly associated with the strength of the MRI systems, the time spent close to the bore, and the workers' speed of movement. Whether there are long-term health consequences from these acute neurobehavioral symptoms is unknown.[16]

In general, there is very little scientific literature on the long-term adverse health consequences for health care workers in the MRI field. There is a lack of consistent evidence of cancer risks in industrial groups exposed to static magnetic fields (among other hazards) or of reproductive effects based on the few limited studies of female MRI workers.[17]

7.3.2 Radiofrequency thermal ablation

Radiofrequency ablation (RFA) procedures in medicine are mainly used in cardiology for the treatment of cardiac disorders and in oncology for tumour treatment.[18]

For interventional cardiology, RFA is a minimally-invasive medical procedure used to correct irregular heart rhythms (primarily atrial fibrillation). The RF device consists of an ablator (catheter), RF generator, and a control console.[19] The energy-emitting probe (electrode) is at the tip of a catheter which is inserted through very large veins into the heart. Ablation involves destroying small diseased parts of heart muscle by means of the resistive heat due to the electric current generated by high frequency RF waves in the catheter.

RF is also used to treat tumours in lung, liver, kidney, and bone but with the generator at a higher power than used for cardiology purposes. A needle-like RFA probe is placed inside the tumour.[20] RF waves passing through the probe increase the temperature within tumour tissue resulting in its destruction. RFA may be combined with locally delivered chemotherapy treatment, and it is of particular value in reducing the size of inoperable tumours.[21] RFA is minimally invasive and repeated procedures can be done with few complications when performed under radiological guidance.

7.3.2.1 Adverse health effects of patients undergoing RFA procedures

Generally with RFA, unhealthy tissue is treated by thermal means at RF frequencies up to 200 MHz. However, the heat is generated in a small area. Temperatures in the treated areas could reach 100°C or slightly higher. Some complications are associated with RFA, but they are usually reversible.

The main adverse effects of RFA treatment are reported in the literature to be thermal consequences resulting from direct or indirect RF heating of tissue.

The following thermal effects on patients have been reported after use of tumour therapy:

- Thermal injury to the ureter following ablation of renal cell carcinoma[2]
- Case reports of skin thermal necrosis after treatment of osteoid osteoma[12]
- Non-target thermal damage to adjacent structures after treatment of liver, pulmonary, and renal tumours[19-23]
- Cardiac complications that can arise from thermal injury due to RFA such as esophageal temperature increase during pulmonary vein isolation.[24]

In general, the reported thermal effects have responded to treatment and did not lead to further complications. At relatively low levels of exposure to RF waves (levels lower than those that would produce significant heating), there is no evidence for long-term health effects on patients.

Precautions necessary for RFA are to ensure vulnerable patients are not adversely affected by the procedure and to adopt appropriate techniques of treatment to prevent excessive heating of non-target organs (such as those adjacent to tumours.)

7.3.2.2 Occupational health risks associated with RFA

We have not found literature concerning adverse health effects for acute or chronic exposures of RF associated with ablation procedures to hospital staff, particularly for physicians who are the most exposed to RF.

7.3.3 Localized dielectric heating (shortwave diathermy)

Shortwave diathermy is the therapeutic application of high frequency alternating current used in physiotherapy treatments. RF fields are used to speed up the healing of tissues by providing deep heat to a large area of the body positioned under conductance plates.[23] Continuous shortwave diathermy is the technique of choice when heating of deep tissue is required. Diathermy also allows superficial structures to be heated selectively by means of various surface heating techniques. Sub-acute or chronic conditions respond best to continuous shortwave diathermy which, when used properly, can be as effective as high power ultrasound. Diathermy is used to relieve pain and muscle spasm, resolve inflammation, reduce swelling, increase joint range and decrease joint stiffness.[24]

Measurements made of RF fields close to diathermy equipment show that for continuous wave shortwave equipment, recommended ICNIRP whole body levels were

exceeded 0.5–1.0 m from the electrodes and cables. This distance was reduced to 0.5 meters for microwave units and pulsed shortwave diathermy models.[25]

7.3.3.1 Adverse health effects of patients undergoing diathermy

No published reports could be found concerning chronic effects related to patients' treatments with diathermy. An important precaution when administering shortwave diathermy is to ensure the heating is targeted accurately by using correctly positioned applicators.

7.3.3.2 Occupational health risks associated with diathermy

Physiotherapists can be exposed to elevated levels of RF during diathermy treatments if they work closely (less than one meter) to the electrodes and cables of the units.[25] Studies on long-term occupational health effects for physiotherapists have mainly focused on adverse reproductive outcomes.

Cancer: No literature was available on cancer risks for physiotherapists or other health care workers associated with occupational exposure to diathermy.

Reproductive outcomes: Studies on reproductive outcomes and occupational exposure have been conducted on physiotherapists using shortwave and/or microwave diathermy. Measurements of shortwave and microwave diathermy equipment exposures vary considerably depending on the equipment and location of the operator. Exposures above current recommendations have been documented, particularly within 0.5 meters of the device.[26] Four case-control studies have been conducted. Ouellet-Hellstrom et al. compared 1753 miscarriages and 1753 control pregnancies recruited via mailed questionnaire to female registrants of the American Physical Therapy Association.[27] Self-reported number of treatments administered, using both shortwave and microwave radiation per month, were used to categorize women into exposure categories. An overall increased risk of spontaneous abortion was found for use of microwave diathermy: odds ratio 1.28 (95% confidence interval 1.02–1.59). An increased risk was not found with reported use of shortwave diathermy equipment.

Ouellet-Hellstrom et al. collected their data in 1989; since then, use of microwave diathermy has declined substantially in favor of shortwave diathermy: a 2007 survey of British hospitals confirmed that there were no microwave diathermy units in use.[31] Safety guidelines for physiotherapists consistently suggest operators stand away from the patient during treatment, but the recommended distances vary from 0.5 to 1.5 meters and are based on avoiding exposures above ICNIRP limits.

Takinen et al. (1990)[28] conducted a nested case-control study of physiotherapists in Finland who had become pregnant in the 1973–1983 study period. Cases were derived from the medical registrar, and exposure information was based on recall of equipment and procedures used. The odds ratio of spontaneous abortions occurring

after 10 weeks of pregnancy was significantly elevated (OR 2.5; 204 cases) for use of shortwave diathermy but did not remain significant after adjustment for occupational variablers and lifestyle confounders. However, for congenital malformations, shortwave diatherapy administered for at least 1–4 hours per week remained statistically significant (OR 2.3, 95% CI 1.1–5.2; 46 cases) after adjustment for confounding, but the highest exposure category showed no effect. Inconsistencies in dose-response and potential misclassification of exposure suggest further study is needed. The remaining two studies[29-30] had much smaller samples, did not distinguish between microwave and shortwave equipment, and failed to find statistically significant findings.

Cardiovascular disease: A 1983 cross-sectional study of American male physiotherapists found an increased prevalence of self-reported cardiovascular disease depending on use of microwave and shortwave diathermy.[32] However, these findings were not replicated in subsequent studies.

Cataracts: The lens of the eye is known to be sensitive to heat compared to other organs; however, we found no epidemiological data linking RF occupational exposure for physiotherapists to an increased risk of cataracts.

7.3.4 Other medical and paramedical RF uses

RF surgery is commonly used in dermatology for resolving skin disorders. The combination of using diode laser and bipolar RF energy is an effective modality for the treatment of superficial and deep acne scars.[33] RF treatments are a preferred method for dermatologists because of the minimal skin damage induced by this technique.[7,22] Some of the advantages of the RF technique are:

- the use of low RF intensity to control temperature rise during the procedure in order to prevent overheating of the treated area
- the use of high-frequency RF waves to limit the penetration of RF waves inside the skin
- the limited impact of RF energy on the surrounding healthy tissue as only the tip of the electrode comes in contact with the tissue for a short time.

RF devices are also used in paramedical aesthetics for the treatment of irregularly pigmented skin, acne, rosacea, psoriasis and other skin disorders using RF devices.

7.3.5 Comparison of medical sources of EMF to consumer devices

Exposure to RF from consumer devices differs in many ways from exposures from medical applications reviewed here. Some of the characteristics that differ include:

- ***Frequency:*** Consumer products such as mobile phones, blue tooth, laptops, baby monitors, and smart meters emit and receive RF waves at high frequencies

ranging from 900 MHz to 2.45 GHz, while the medical devices use lower frequencies up to 200 MHz (which penetrate more deeply into tissue).

- ***Output power:*** Consumer products use very low power, generally below 1 Watt on average, while medical applications require powerful sources of EMF, as shown in Table 1.
- ***Duration of exposure***: Although the exposure of patients to medical EMF is substantially higher than established limits, it lasts only for the brief course of the examination or treatment. Health care workers may experience transient higher levels of EMF in the course of their work, and also may be exposed at low levels during the course of their work day. The general public is regularly exposed to very low levels of ambient EMF over 24 hours.
- ***Distance from the EMF source***: For most medical uses of EMF, patients are exposed to the near field, which has the highest EMF output power. For the public, higher levels of near-field RF exposure can only occur from personal use of wireless phones next to the head, but at much lower levels than experienced by patients exposed to medical devices.

As such, any demonstrated health effects related to RF/EMF exposure to patients and medical staff cannot be directly related to the type of exposures to RF received by the general public.

7.4 Research Gaps

There is a lack of follow-up studies on the long-term health consequences for patients exposed to relatively high levels of RF from diagnostic and therapeutic use of medical devices.

Exposure assessment and epidemiological studies of health care workers exposed to RF, particularly those involved in MRI, ablation and diathermy procedures, are needed to determine the likelihood of health consequences related to acute and long-term RF exposures in their work environment.

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Section 8

Health Effects Associated with Exposure of Industrial Workers to Radiofrequency Waves

Table of Contents

Summary

- Industrial applications of RF include microwave drying, induction and dielectric heating, broadcasting applications (AM, FM, CB, and TV) and radar; however, exposure assessment has been only done on several of these RF-emitting sources and there are even fewer epidemiological studies of health effects associated with specific industrial sources.

- Well-recognized health effects of acute high level industrial exposures to RF are heating of body tissues (thermal effects) and radiofrequency (RF) induced contact shocks. Occupational exposure limits are designed to prevent these effects. Case reports of acute industrial exposure to RF describe the immediate effects of accidental over-exposure (generally without direct measurement of the level of those exposures), and in most cases with no reported long-term follow up.

- For the most part, workers exposed to RF in the dielectric heating industries have reported similar symptoms to that of non-exposed comparison workers; however, sometimes paresthesia (a burning or prickling sensation that is usually felt in the hands, arms, legs, or feet) is reported more often in exposed workers.

- Brain tumours and cancers of the blood such as leukemia and Hodgkin lymphoma are the most extensively studied cancer outcomes in studies of long-term occupational RF exposure. Overall, observational studies have not shown an increased risk for any cancer site although a few studies have shown some indication of an excess in leukemia in military personnel exposed to radar.

- Studies of cardiovascular mortality in RF-exposed workers have been consistently negative.

- Military personnel were the focus of several studies of the effects of occupational exposure to RF on semen parameters. Although there was some indication of adverse sperm effects, the recruitment of subjects in these studies were either poorly described or there were poor participation rates.

- The few studies on the risk of eye cataracts following occupational RF exposures have shown mixed results.

- The quality of exposure assessment and the relatively small numbers of workers studied are major limitations of observational studies of occupational exposure to RF.

- Further research into health effects associated with occupational exposures to RF is needed, both for what can be learned of the risks of occupational exposure and for what it says about high level exposures in general, given that workers may be exposed to RF at a greater intensity and for longer duration than the general public, and because their exposure may be to lower frequencies of RF which can penetrate more deeply into the body.

8.1 Introduction

There are numerous applications of RF fields in industry. Studies of workers in these industries may provide useful insight into the health risks associated with unique types and levels of exposure to RF.

Many of these applications, such as radar and plastic welding, pre-date by decades the widespread use of mobile phones, permitting assessment of exposures of very long duration.

This section describes principal industrial uses of RF waves and evaluates the literature concerning acute and chronic exposures of industrial workers to RF and associated health effects.

8.2 Industrial Applications of RF

8.2.1 Industrial microwave ovens (dryers)

Industrial microwave ovens use the same principle for heating as household microwave ovens and are generally used for drying wet surfaces, such as building components (ceilings, wall surfaces) and flooded surfaces. They operate at higher power than household ovens (which range from 0.5 to 2 kW) at levels from 1 kW to 5 kW and use 2 frequencies: 915 MHz (wavelength 30 cm) and 2.45 GHz (wavelength 12 cm), which is similar to consumer ovens.

8.2.2 Induction heating

Induction heating is a non-contact heating process that heats conductive material by exposing it to alternating electromagnetic fields. A rapidly alternating magnetic field induces eddy currents in a conductive material placed in its vicinity, heating the material by induction. Induction heating is used to bond, harden or soften metals or other conductive materials. Induction heating is commonly used in several applications in the aviation and automotive industries, in pipe fitting, shipbuilding and foundries. Induction heating uses frequencies ranging from 100 to 500 kHz and powers up to 500 kW.

8.2.3 Dielectric heating

Dielectric heating is a technique used for heating nonconductive materials from the inside to high temperatures by means of high-frequency alternating continuous RF fields. It is commonly used for welding plastic parts, sealing plastic bags, drying and bending pieces of wood, drying ceramics, sterilizing foods, pre-vulcanizing rubbers, drying and bonding textiles and other such uses.

The frequencies used in dielectric heating range from 5 MHz to 80 MHz and powers from 5 to 450 kW.

8.2.4 Installation and maintenance of mobile phone base stations

Mobile phone base stations are used in telecommunications to send to and receive RF signals from mobile phones. The frequencies used are usually from 900 MHz to 2.45 GHz while the powers range from 1 W for antennas inside buildings to 40 W for antennas sited at high elevations.

The installation and maintenance of mobile phone base stations is supposed to be conducted with the RF beam turned off, thus with no risk to workers.

8.2.5 Broadcasting applications: AM, FM, CB, and TV

RF waves are largely used for radio and television broadcasting. Radio broadcasting stations emit in different frequency and power ranges, depending on the type of emissions. Amplitude modulation (AM) radio operates at frequencies from 550 to 1600 kHz while frequency modulation (FM) radio uses frequencies from 88 to 108 MHz. Both AM and FM use a range of powers from few hundred Watts to 45 kW depending on the scale of the areas covered. Citizens band (CB) radio operates at 27 MHz and uses a power of 4 W. TV broadcasting stations emit in the 470–854 MHz range at a power close to 1 Megawatt (MW). Radio and TV broadcasting installations are generally considered safe work places. However, when working close to antennas for maintenance or repairs, precautions must be taken to avoid over-exposure.

8.2.6 Radar

Radar systems are used for detecting objects and measuring the distance separating them from the RF antenna (ranging). Radars transmit RF waves by directive antennas aimed towards a target; a portion of the RF energy is reflected back to the radar, thus potentially exposing the operator. Radar emissions can be continuous (cw radar) or pulsed (pulsed radar).

The main uses of radar is in air traffic control, air navigation, ship safety, speed limit enforcement on roads, weather monitoring, and military applications.

Radars use a typical power of 1 Kilowatt (kW) and their frequencies range from 3 MHz to 40 GHz, depending on the type of use.

8.3 Occupational Risks Associated with RF

8.3.1 Methods

A literature search was conducted to identify peer-reviewed articles relating to occupational exposure to RF and its health effects. Two databases, Medline and EBSCO were used. Key terms used were: radio waves, microwaves, electromagnetic radiation, electromagnetic field, occupational exposure, occupational diseases, as well as specific industries: plastic welders, amateur radio operators, broadcast station and radar. There were no date limits, but studies were limited to English only. Three literature reviews of

observational studies of RF which included occupational exposures were identified: Breckenkamp et al. (2002), Ahlbom et al. (2004) and Habash et al. (2009).[1-3] These reviews included most of the observational studies identified in the literature search, with the exception of a 2006 case-control study done as part of the Interphone project,[4] a 2009 retrospective cohort study on military radar operators[5] and a small 2007 case-control study on non-Hodgkin lymphoma involving exposure to both ionizing and non-ionizing radiation.[6]

8.3.2 Assessment of occupational exposures to RF

Exposure assessment is consistently reported as the greatest limitation to the interpretation of studies on the effect of both acute and chronic occupational exposure to RF.[7] Acute exposures to RF typically involve accidental exposures with exposure estimates based on reconstruction of the event.

Epidemiological studies of chronic exposure most commonly use job titles to assign workers to exposure categories. The precision of exposure categories varies widely and may be based on measurements assigned to groups of workers or the expert opinion of industrial hygienists used to estimate exposure for a given worksite or job title or on self-reported exposure to workspace or source equipment.

In reviewing studies on the health effects of occupational RF exposure, important considerations are the factors that affect exposure to RF and the fact that RF exposure does not usually occur in isolation from other exposures to EMF, such as Extremely Low Frequency radiation or to industrial contaminants such as metals or ionizing radiation. As such, it is difficult to attribute health outcomes to RF exposure alone. The majority of the studies on health effects of occupational exposure to RF do not contain information on exposure measurements nor do they contain enough information about the factors that have an effect on personal exposures, as described in Section 5:

- Output power of the RF source, number of RF sources
- Whether an antenna is directional or omnidirectional
- Frequency of RF waves
- Duty cycle of the RF generator
- Continuous vs. pulsed waves
- Distance and location of the worker from the RF source (e.g., in the radiated lobe of source)
- Presence of barriers, reflective surfaces (i.e., that either decrease or increase exposure)
- Duration of exposure, frequency of exposure
- Whether the exposure is to the whole body or is localized.

Occupational exposures to RF are much different from public exposures in that occupational populations are potentially exposed to much higher RF power densities. Other than broadcast or mobile phone base station operators, most other workers (e.g., police using radar guns, RF sealers/plastic welders, and radio/telegraph workers) are exposed to RF in frequencies outside those normally found for public exposures and therefore any exposure information obtained about these populations are not directly applicable to public health. At lower wave frequencies, experienced by RF plastic welders and telegraph workers, RF penetrates deeper into tissue and below 110 MHz, contact currents may develop, whereas in the general population, contact currents are rarely a concern.

Radar emissions include the frequency range of interest to public health, although source output power levels and therefore occupational exposures are documented as being much higher. Richter et al., 2002 reviews five case reports of military personnel where output power levels ranged from 100 to 300 W and radar frequencies included MHz to GHz ranges.[8] Measurements of radar main beams by Puranen and Jokela (1996)[9] found radar peak output power levels ranging from 125 kW to 3000 kW for stationary radar antennas.

There is a dearth of studies that measure RF exposure to workers. Seventy percent of the studies reviewed are older than 10 years (prior to 2002). Since that time, the technology of exposure assessment has improved and the measurements made in the past may not be as accurate or reliable as measurements made presently. The most promising occupational populations to study for relevant health effects to the public are those who are exposed to frequencies and intensities that are similar to those affecting the public, i.e., broadcast or base station workers. Unfortunately, most of the studies done of these workers were case reports with exposure ascertainment conducted after accidental exposures, with attempts at reconstructing the accident situation rather than measuring more typical exposures. The exception is the exposure assessment study by Alanko and Hietanen (2007) which describes common exposures to broadcast tower workers.[10] Measured exposures were between 0.1 W/m^2 (0.01 mW/cm^2) and 2.3 W/m^2 (0.23 mW/cm^2) for GSM and radio antenna workers (which are well below ICNIRP reference levels).

Accidental exposure to RF was described in two case reports.[11,12] Schilling described three TV antenna installers who were accidentally exposed to RF of 785 MHz frequency for up to five minutes.[11] The survey meter reading reached the full scale of 20 mW/cm^2 at 10 cm from the antenna, but the exposure was most likely higher. In another case study cited by Hocking and Westerman (2001),[12] a rigger was exposed to a CDMA mobile phone station antenna that should have been turned off. His exposure was estimated by reproducing the conditions of the exposure at a later date in the laboratory. The RF level from the antenna at a power of 4 W and frequency of 878.49 MHz was estimated to be only about 0.015–0.06 mW/cm^2 for an exposure of over 1–2 hours.

In summary, exposure ascertainment for occupational sources of RF is rather crude, and important determinants, such as output power and number of RF sources, pulsing of the wave, distance of the worker from the RF sources and duration and frequency of exposure, are often not described. When measured, power output levels (W) can vary widely, as can power densities (W/cm^2).

Table 1 provides exposure assessment information which derives mainly from epidemiological studies concerning effects of workers' chronic exposure to RF. Only studies presenting quantitative exposure measurements were included.

Most of the studies reviewed used area measurements and distance from the source to determine a range of typical chronic exposures. A variety of measurements were done for EMF, including power (W/m^2), magnetic B fields (μT), current densities (mA/m^2) and electric fields (V/m). Military personnel exposed to radar and plastic sealing/welding workers tended to incur higher exposure than allowable levels. The few studies measuring exposure to RF for broadcast/antenna workers were consistently below recommended limits for occupational exposure.

Appendix A describes the current Canadian occupational safety regulations and standards for occupational exposure to RF, including recommendations for precautionary measures for workers exposed to RF.

Table 1. RF exposure measurements of various industrial occupations

Study	Job/Location (Type of study)	Description of Job/Area	RF Frequency	Methods	Exposure	Comments
Alanko and Hietanen (2007)[10]	Antenna/ broadcast workers; Finland Exposure assessment study only	Typical working tasks around or inside antenna masts include antenna maintenance, painting, tightening the bolts, beacon replacement, and tower rigging and replacement. Mast 1: 82 m high where workers climbed inside tower; Mast 2: 62 m high where workers had to climb outside of the tower	Mast 1: GSM 900 and GSM 1800 cellular phone networks, and also local radio and amateur radio antennas Mast 2: Only GSM 1800 antennas	Measurements made 2.5 and 3.0 m intervals in a vertical direction, depending on tower type	Mast 1: highest densities at heights of the base stations. For GSM 900 at 63 m and GSM 1800 at 70m, < 0.1 and 0.2 W/m^2, respectively. Increase in power density near the top was due to amateur radio antennas on top of tower (highest instantaneous power density was 0.4 W/m^2 in the climbing space). Mast 2: Two antennas at 28 and 30 m, maximum 0.9 W/m^2. Maximum instantaneous was 2.3 W/m^2, recorded during maintenance tasks of the tower. Below ICNIRP reference levels of 22.5 W/m^2 at 900 MHz and 45 W/m^2 at 1800 MHz.	Exposures were low when ladders are inside the tower, but are higher when the ladders are located outside. According to siting instructions, the antennas should not be directed to pass through the climbing space.
Cooper et al. (2004)[7]	High power –TV and radio broadcast; UK Exposure assessment study only N=27	FM Radio – ERP was 250 kW per channel UHF television – 500 kW per channel at top of 300 m mast	FM Radio UHF television	Personal monitor (incorporated a shaped response to give electric and magnetic field strengths as a percentage of ICNIRP levels) worn by engineer close to high-power VHF antennas	Median – 23.3; Mean – 24.6 (95% CI 19.6–29.6) percent of ICNIRP levels.	Field strengths rarely constant for more than one minute, indicating either power output of transmitters were not constant or position of the monitor was constantly changing.
Cooper et al. (2004)[7]	Medium power broadcast and telecommunications; UK N=15	VHF/UHF 100–200 W with antennas mounted on top of 45 m tower		Personal monitor (incorporated a shaped response to give electric and magnetic field strengths as a percentage of ICNIRP levels)	Percent of ICNIRP levels Median – 10.6; Mean – 10.4 (95% CI 7.8–13.0)	Use of a portable receiver/ transmitter was captured by the personal monitor.

Study	Job/Location (Type of study)	Description of Job/Area	RF Frequency	Methods	Exposure	Comments
Cooper et al. (2004)[7]	Low-power broadcast and telecommunications; UK Mobile phone base stations and other lower-power transmitters (unspecified)	Mobile phone stations	Unspecified frequency	Personal monitor (incorporated a shaped response to give electric and magnetic field strengths as a percentage of ICNIRP levels)	Percent of ICNIRP levels: Median – 9.4; Mean – 8.6 (95% CI 5.5–11.8)	Field strengths generally did not exceed detection threshold, and any that did were brief and of low intensity.
Jokela and Puranen (1999)[13]	Broadcast antennas – UHF-TV and FM antennas	Working near or climbing through transmitting antennas.	TV and FM (50–800 MHz) average power from 10 to 50 kW	Electric field measured inside a section of mast surrounded by a typical dipole-panel type FM antenna	Maximal power density up to 50 W/m^2. Field distribution is highly non-uniform, but average over whole body is above the 10 W/m^2 limit. The 10 W/m^2 level can be exceeded at 50 m and the 100 W/m^2 can be exceeded at 10 m for UHF-TV and FM antennas when a new mast is being built near an old one that is transmitting.	Occupational limits commonly exceeded. Usually for UHF masts, only accidental exposures are possible since entering the radome of the mast is strictly prohibited.
Grajewski et al. (2000)[14]	RF heater/sealer operators; USA Cross-sectional study 27 RF- exposed men and 14 unexposed men	RF sealers and dielectric heaters are used to heat, dry, emboss, melt, seal, or cure materials that are poor. Electrical conductors (dielectric)	12–57 MHz (93% of machines between 20.3 and 32.0 MHz)	Broadband field probes, E and H field strength at eye, chest and groin level, induced current from E- field and frequency. Induced current.	Geometric mean E field ranges (exposed): (1.2 to 9.0) x 10^3 V^2 /m^2 (35 V/m to 95 V/m); B field: (1.9 to 6.4) x 10^{-2} A^2/m^2 (0.14 to 0.25 A/m) Vs. ND for controls. Average induced current 0.7 to 1.3 x 10^2 A vs. ND for controls.	.

Study	Job/Location (Type of study)	Description of Job/Area	RF Frequency	Methods	Exposure	Comments
Bini et al. (1986)[15]	Plastic sealers; Italy Cross-sectional study – operators in room with 67 sealers	Sealers make thermal seams in plastic-sheet articles like inflatable boats.	27.12 MHz and 13.56 MHz Duty cycles of 10% to 70%, entire cycle duration is 1 to 6 minutes in 83% of units.	Measurements made in a room lined with steel sheets to prevent electromagnetic interference from other RF sources. Field strength measured at height of head, abdomen, and hands of operator.	RF-on times are short (a few seconds). At hands, 70% of sealers were above 300 V/m and some up to 4000 V/m. At abdomen, 50% of units were above 300 V/m and at head 70% were above 300 V/m with maximums of 1000 V/m. Exceeded Italian guidelines for electric fields but confined to immediate vicinity of units.	
Wilen et al. (2004)[16]	RF plastic sealers; Sweden Cross-sectional study 46 RF sealers operated by 35 RF operators were measured.	RF is used to produce to heat to seal plastic for things like plastic clothing, tents, and covers. Usually exposure times are for 1-10 secs.	27 MHz	Electric and magnetic field strengths were measured in 7 positions: head, trunk, waist, knees, feet and both hands. Contact currents measured.	Mean electric field and magnetic field averaged over entire body (SD): 88 (102) V/m and 0.19 (0.19) A/m, respectively. Maximum was 2 kV/m and 1.5 A/m at hands. Induced current 101 (147) mA as sum of both feet. Mean value in wrists was 102 (1146) mA.	16 of 46 workplaces exceeded Swedish standard; 11 exceeded ICNIRP levels.
Kolmodin-Hedman et al. (1988)[17]	Plastic welders; Sweden Retrospective cohort study – 113 exposed, 23 control workers	Machines include tarpaulin, ready-made, and automatic.	25-30 MHz	E and B fields measured in frequency range 25 to 30 MHz at least 0.5 m from worker. Measured at area of right and left hands, abdomen, inguinal region, right and left knees, right and left feet (5 times at each location).	50% of welding machines exceeded present Swedish ceiling level of 250 W/m^2. Highest leakage in the ready-made clothing industry.	
Lagorio et al. (1997)[18]	Plastic-ware workers; Italy Retrospective cohort study 302 women and 4 men	Sealing of lifeboats, dinghies, and a few other polyvinyl chloride products.	No frequencies mentioned.	Quantitative RF exposure assessment was considered unattainable.	Findings from mid-1980s survey before metal-shielding or earthing of sealers were adopted showed that levels often exceed10 W/m^2.	

Study	Job/Location (Type of study)	Description of Job/Area	RF Frequency	Methods	Exposure	Comments
Jokela and Puranen (1999)[13]	Plastic sealers Review of exposure assessments		27 MHz (HF sealers for PVC) 13 MHz (glue dryers)	Description from other surveys.	Peak electric field of 2650 W/m^2 (265 mw/cm^2); 600 mA induced current from feet; high local SAR about 20 W/kg per 100 mA (through one foot), maximal SAR peaks may be up to 100 W/kg. Whole body SAR varies from 0.12 to 2 W/kg with 1000 V/m maximal E field.	Exposure assessment is difficult since the operator is in the near field.
Lotz et al. (1995)[19]	Police officers/traffic radar devices; US Exposure assessment study, feasibility study	Use of 10 fixed and hand-held traffic radar devices	24.15 GHz and 10.525 GHz emitting less than 100 mW	Used power density meters, with frequency specific power sensors and standard gain horn antennas, frequency counters, survey meters, and voltmeters. At aperture and 5 and 30 cm in front of antenna, around and behind unit and in the position of operator (head and groin level in absence of operator and at eyes, waist and knees in presence of operator).	Ranged from less than minimum detectable level (MDL) < 0. 020 to 2.60 mW/m^2 (at waist) when radar gun was resting on passenger seat. Maximum measured at aperture (3.0 mW/m^2).	Only in main path were levels above minimum detectable level.
Jokela and Puranen (1999)[13]	Radar	Mechanics testing and maintaining radar systems, soldiers using tactical radars, and occasionally other people working in locations where high power radars are used. High power in a narrow beam and scanning.	3 GHz 9 GHz Power: 125 kW to 3000 kW		In the stationary beam, power density commonly exceeds 100 W/m^2 and may be up to 1000 W/m2 in front of the antenna. Occupational limit of 50 W/m^2 may be exceeded at distances of several hundred metres from antenna. Most exposures happen outside the main beam. For high power air surveillance, average power density seldom is above 1 W/m^2. In tactical radars, where antenna is close to operators, the exposure may exceed 10 W/m2 but not 100 W/m^2.	

Study	Job/Location (Type of study)	Description of Job/Area	RF Frequency	Methods	Exposure	Comments
Szmigielski (1996)[20]	Military personnel; Poland Retrospective cohort study Mean number= 127,900	All jobs in military 1971-85	150-3500 MHz pulse-modulated	Exposure data taken from health hygienic services of military. Exposure rate hard to establish.	80-85% did not exceed 2 W/m² (0.2 mW/cm²) and others were 2-6 W/m², Exposures exceeding 6 W/m² were registered incidentally.	Daily, monthly exposure was difficult to assess. Not sure how exposure measurements were originally conducted.
Tynes et al. (1996)[21]	Seagoing female radio and telegraph operators - 2619 women; Norway Nested case control study	1961-1991. Exposure to RF in radio rooms ascribed to leakage from unshielded feed lines between antenna and transmitters. Radio officers usually 1-2 meters from transmitters and feed lines.	405 KHz to 25 MHz Also ELF 50 Hz	Operated transmitters at maximum power. Unmodulated transmitted power for telegraphy between 410 and 535 kHz was 1.5 kW. Unmodulated and amplitude modulated telephony were 400 W between 1.6 and 3.6 MHz and 1.5 kW in range 3.6-25 MHz. A distance of 0.5 m was maintained between a field probe and any person was maintained.	At operator desk, below the limit of detection (~20 V/m) at all frequencies, 0.05 A/m for > 3 MHz and 0.15 A/m below 3 MHz. At 0.5 m from tuner (representing worst-case scenario) and 1.5-2m above floor level, E field was 70-200 V/m and H field was 0.1-0.5 A/m, increasing with frequency. Close to unshielded antenna field lines, extreme values of 1400 V/m and 2.5 A/m.	
Skotte (1984)[22]	Danish merchant ships Exposure Assessment study only of telegraphy and telephony equipment	85 measurements of electrical (E) and magnetic (H) field strengths close to 12 radio transmitters	Range of 400 kHz to 25 MHz	Transmitted power from 50 to 200 W Loop antenna (for H-field values < 10 MHz) and HL instrument with probe parallel to the H-field	Ratio of E-field or H-Field squared divided by ANSI standards: Highest values measured at 0.25 m from antenna field line. Range: Ratio of E-field 0.001 to 31 Geometric mean: 0.0089 to 2.3 Range: Ratio of H-field 0.001 to 12 Geometric mean 0.011 to 0.68	Exposure to RF was dependent on the distance between the feed line and the operator and should be < 0.5 for exposure to be below standards.

Converted using: http://www.compeng.com.au/emc_conversion_tables_field_strength_calculator.aspx

8.3.3 Effects of acute occupational exposures to RF

There are two well recognized health effects of acute high level exposures to RF: heating of body tissues (thermal effects) and RF-induced and contact shocks. Exposure to RF at lower frequencies can induce a current in the human body causing depolarization of nerve cells and a shock sensation. Additionally, contact with a conductive object polarized by RF can cause a contact shock or burn. Health Canada's Safety Code 6, which covers human exposure to RF in the range from 3 kHz to 300 GHz, limits exposure to prevent these effects.[23] Animal studies demonstrate alterations in core body temperature of about 1˚C at a whole-body average specific absorption rate (SAR) of 4 W/kg. For controlled environments, a safety factor of 10 is applied, resulting in a whole-body average SAR of 0.4 W/kg (in comparison to levels of 0.08 W/kg for the general public). Limits to prevent induced and contact currents vary depending on the frequency of RF and were selected to avoid shocks and burns, though the induced current may be perceptible at levels below these limits.[23] The health effects of exposure above these limits vary, depending on several factors such as variation in field strength, reflection within the body and individual organs' susceptibility to heat. Distance, shielding and insulation are effective methods to prevent hazards related to heating and contact shocks and burns.

Population health studies of mobile phone use include provocation experiments which allow careful determination of exposure, with sham exposures as a control.[24] Analogous controlled experiments have not been conducted using industrial sources of RF. Knowledge of the acute effects of occupational exposure to RF is mainly derived from case series reports. These reports fall into two broad categories: accidental exposures to RF above recommended limits and studies of the worksite of workers with symptoms attributed to RF exposure.

Hocking et al. (1988)[25] described an Australian overexposure accident involving nine radio linemen. In February 1986, the team was dismantling a television bearer. A waveguide, operating at 4.139 GHz, attached to the bearer was inadvertently activated for 90 minutes. Two members of the team within 2 meters of the waveguide were estimated to have been exposed to 4.6 mW/cm^2 for those 90 minutes; the SAR was estimated to be 3.8 W/kg. This was above the Australian exposure standard, and the SAR approached the level at which thermal effects occur. The other seven members were further away and were estimated to have been exposed to RF of less than 0.15 mW/cm^2. The two highly exposed engineers experienced only a warm sensation during the exposure and no effects were found at a medical exam eight days later. The entire team underwent ophthalmological follow up over a nine-month period and no abnormalities were detected. No further follow-up was undertaken.

Reeves (2000) [26] published a review of 34 American Air Force personnel overexposed to RF between 1973 and 1985 and referred to the US Air Force School of Aerospace Medicine for assessment. Exposures involved a variety of communication and radar

equipment and usually resulted from unintentionally leaving equipment active or inappropriately connecting a dummy load to absorb the RF. The frequencies used by the source equipment were not documented or classified for 14 of the cases. The author does not report all the remaining frequencies, but notes that in three cases, equipment used frequencies at 9, 20 and 235 MHz. Estimated power densities varied from below 25 mW/cm^2 to greater than 1500 mW/cm^2; estimates of SAR were not reported. Fourteen workers became aware of the overexposure because of sensation of warmth; several did not become aware of the situation until noting a switch had been left on, or equipment had not been properly connected. Extensive clinical and laboratory assessments failed to demonstrate changes in blood counts, liver and thyroid function. The majority of cases—28—were assessed once; eight others were seen for at least one additional visit. Thirty of the exposed workers underwent psychological assessment due to concerns about mood changes or short-term memory impairment. All abnormalities detected were attributed to pre-existing conditions such as learning disabilities or personality traits; however, at question is the validity of this finding given that there were no baseline data to compare with the assessment results.

In contrast, Schilling (1997)[11] describes the long–term effects of accidental over-exposure in the case of three antenna engineers working on a 785 MHz RF television antennas. Their skip (lift) was wound up instead of down, which exposed them for a few minutes to the near-field of the antenna; their badges registered the full scale of 20 mW/cm^2 and the exposure was likely much higher. After initial erythema, the workers developed symptoms including severe headache, numbness, paresthesia, and malaise, and the headaches persisted during the three to four years of follow up.

In summary, whether or not long-term effects result from acute occupational exposures to RF is difficult to assess without further information on the characteristics and levels of actual exposures at the time of the incident as well as the thoroughness of follow up. Because a mechanism for effects other than thermal effects is unclear and given inconsistent symptom reports, exposure limits have been based only on preventing thermal effects and RF shocks as adopted by Canadian and international organizations.[2,23]

8.3.4 Observational studies of industrial workers chronically exposed to RF

Observational studies of health effects associated with chronic occupational RF exposure include several outcomes:

1. Symptoms
2. Cancer, with most research focusing on brain and hematopoietic cancers
3. Adverse reproductive outcomes, primarily male semen parameters
4. Cardiovascular disease mortality
5. Cataracts

Symptoms: A 2004 Swedish cross-sectional study of 35 RF plastic sealer operators and 37 controls, included exposure assessment of the electric and magnetic field strength "leakage," as well as induced and contact currents.[16] Out of 46 of the plastic sealer units, 11 exceeded ICNIRP reference levels. Examination of the operators showed indications of diminished two-point discrimination ability (2-PD), but the prevalence of any symptom did not differ from controls. For another study of plastic sealer operators,[15] comparison of the health status of 30 exposed operators and 22 unexposed controls showed the prevalence of eye irritation and upper limb paresthesia were significantly higher in the exposed group. Of the 62 female Swedish plastic welders, 53% reported numbness (paresthesia) in the hands in comparison to 22% of the 23 sewing machining operators and assembly worker controls.[17] Diminished 2-PD was significantly greater, affecting 39% of all 113 men and women operators (versus one of the 23 controls). With further measurement of a subset of workers, reporting numbness or demonstrating diminished 2-PD, 12 of 38 had slower conductive velocity. Exposure assessment of the plastic welding machines found more than 50% exceeded the ceiling values for power density of 250 W/m^2.

Overall, there is some indication that RF exposures to workers in the dielectric industry, may result in a greater likelihood of paresthesia. Whether it is transitory or indicative of pathology needs to be determined.

Cancer: As part of the Interphone case-control study, occupational exposures for 747 cases of glioma and meningioma were compared with 1,494 controls.[4] Detailed interviews about previous employment up to two years prior to diagnosis were used to categorize workers into exposure groups based on scientific literature and a review by two industrial hygienists. Occupational exposures that were thought to exceed the exposure limits for the general public (0.08 W/kg) were categorized as "high" exposure and included dielectric heating equipment users, telecommunication antenna technicians and ham radio operators. Only 87 subjects met the criteria for "high exposure" while more than 85% of the cases and controls were classified as "not exposed." After adjusting for socioeconomic status, area of residence (urban or rural), ionizing radiation exposure, smoking history, and age at diagnosis the odds ratio (OR) comparing the high exposure and no exposure was not statistically significant, at OR 1.22 (95% confidence interval [CI] 0.69–2.15). Job titles can be poor surrogates of exposure, particularly as duties and exposure to RF-emitting equipment varies.

Navy personnel, and civilian populations (amateur radio operators and employees of a wireless communication manufacturer) were subjects of retrospective cohort studies examining the risks of mortality and cancer incidence associated with occupational exposures to RF. Szmigielski (1996) determined cancer morbidity in Polish military career personnel enrolled from 1971–1985. Of approximately 128,00 persons each year, about 3,00 (3%) were considered occupationally exposed to RF. Observed/expected ratios (OER) for cancer morbidity, comparing the overall morbidity rates of the exposed personnel to the non-exposed personnel, was 2.07 ($p<0.05$). Higher OERs were found for

neoplasms of the alimentary tract, brain tumours and malignancies of the lymphatic organs and haemopoietic system (leukemias and non-Hodgkins lymphoma).

Garland et al. (1990)[27] determined the incidence of leukemia among navy personnel. Information on occupations and service history was obtained from service records between 1974 to 1984 of all active-duty, enlisted white males, for a total of 4.0 million person-years at risk. Leukemia diagnoses from this cohort were obtained from the Naval Health Research Center and standardized incidence rates (SIR) were calculated using the American male population as a reference. The authors calculated SIRs for the naval job titles for which there was at least one case of leukemia, using the total Navy population as a reference. Overall, there were 102 cases of leukemia; the age-adjusted incidence rate amongst navy personnel was similar to the national population, 6.0 and 6.5 per 100,000 person-years, respectively. There were no elevated SIRs as a result of internal comparisons of specific naval job categories; for example, electronic technicians had the highest SIR of only 1.1 (95% CI 0.4–2.5). However, the results may be biased as cases diagnosed outside of the Navy Health Centre were not accounted for.

A cohort of 40,581 Korean War naval veterans was followed for 40 years in the study by Groves et al. (2002).[28] Personnel were divided into high and low exposure groups (thought to have exposures below 1 mW/cm^2) based on consensus assessments of job title by Navy training and operations personnel. Low exposure groups included radar and radio operators stationed below deck; high exposure groups, which included electronics and aviation technicians, had the potential to exceed 100 mW/cm^2, although their exposures were typically below 1 mW/cm^2. However, actual measurements of worksite exposures were not reported. Mortality data for the cohort, taken from Veterans Affairs, was compared to the American Caucasian population; the high and low exposure groups were compared internally. For the high exposure group, in comparison to the general population, there was no increased risk of mortality from brain cancer or leukemia, with a standardized mortality ratio (SMR) of 0.7 (95% CI 0.5–1.0) and 1.14 (95% CI 0.90–1.44), respectively. However, within-cohort comparisons of high exposed versus low exposed, showed a relative risk of mortality from nonlymphocytic leukemia of 1.5 (95% CI 1.0–2.2). The relative risk (RR) for nonlymphocytic leukemia was statistically significant for, aviation electronic technicians, with an RR equal to 2.2 (95% CI 1.3–3.7). The authors noted a limitation to the study of several occupational carcinogenic exposures not being accounted for, including lead, cadmium and chlorinated solvents.

Degrave (2009)[5] followed a cohort of 4,417 Belgian soldiers posted at a North Atlantic Organization (NATO) anti-aircraft unit between 1963 and 1994. The two large radar systems emitted frequencies between 1 and 10 GHz and modeling of the electric field generated by the units estimated exposures to fields of 100 to 500 V/m, with hotspots of 300 and 1300 V/m. By comparison, NATO standards in the 1960s limited exposure to less than 112 V/m. The comparison group was 2,932 Belgian military personnel who served at the same time in the same place in battalions not equipped with radar. The RR

obtained by comparison of the two groups for neoplasms was 1.22 (1.03–1.47). The exposed group had an increased risk of death from hemolymphatic cancers (11 cases in the exposed group and 1 in the control group) of RR 7.22 (95% CI 1.09–47.9). The authors noted a potential bias in not accounting for the additional exposures to ionizing radiation from some of the radar equipment (which were replaced in the 1970s).

Using federal licensing data, Milham (1988)[29] identified 67,829 amateur radio operators in the states of California and Washington. A total of 2,485 deaths of this cohort occurred between January 1979 and December 1984, a total of 232,499 person-years at risk, and SMRs were calculated using the American male population as reference. There was a significant increase in the risk of acute myeloid leukemia, SMR 1.76 (95% CI 1.03–2.85). Information on exposure characteristics such as duration of registration as an amateur operator and extent of use, or potential confounding factors, was not available.

Morgan et al. (2000)[30] studied a cohort of employees of Motorola, a large wireless communication products manufacturer. A job exposure matrix was created by expert opinion categorizing job title into exposure groups. High exposure groups included field engineers in cellular phone and paging sectors. Mortality data was taken from the National Death Index, allowing researchers to follow workers if they left employment. A total of 195,775 employees contributed 2.7 million person-years during the 1976 to 1996 period. Unlike the naval and amateur radio operators, 44.0% of the Motorola cohort was female. Compared to the American population, there was no overall increased risk of death. Rate ratios comparing high and low exposure were below or near 1.0 for brain cancer and all lymphomas and leukemias and there was no increased risk associated with exposure for greater than five years. An important limitation of this study was the relatively young age of the cohort, with an average age of 42.8 years at the end of the study period.

The study by Tynes et al. (1996)[21] was unique in that exposure measurements were undertaken and cancer incidence was investigated in women, consisting of a group of 2,619 female telegraph and radio operators on Norwegian merchant ships. Measurements were taken in the radio rooms of three ships. The equipment emits RF with frequencies between 1.6 and 25 MHz. Electric field strength was 20 V/m, with elevated levels of 200 to 1400 V/m near the antenna feed lines. The time that workers spent in these rooms was not reported. Using the Norwegian national population as a reference, there were no increases in the incidence of brain tumours or leukemia. However, an increased SIR for breast cancer was found for workers over the age of fifty of 1.5 (95% CI 1.1–2.0). Though women were followed from 1961 to 1991, the median time at sea was only about three years. The authors also note that operators were exposed to other potential risk factors for breast cancer such as shift work. Data on other known risk factors for breast cancer such as smoking, obesity, and family history were not collected.

Within a cohort of 340 police officers, a cluster of six cases of testicular cancer in police officers who regularly used traffic radar guns was reported and all routinely held the radar gun in their lap in close proximity to their testicles. However, no cause and effect association could be determined with such small numbers.[31] An increased risk of ocular melanoma associated with occupational use of radio communication sets was reported in a case-control study by Stang et al.[32] A total of 118 cases and 475 controls were interviewed. An elevated OR of 3.3 (95% CI 1.2–9.2) was found, although there was no relationship with duration of exposure.

A small study by Lagario et al. (1997)[18] on the mortality of 481 female plastic ware workers found a significant elevated risk for leukemia (SMR 8.0, 95% CI 1.0–28.2) but only based on two cases. The effects of exposure to solvents and vinyl chloride monomer could not be ruled out.

Overall, although there are suggestions of an increased risk of leukemia with RF exposure in some occupations, the inconsistent findings and validity issues concerning exposure ascertainment and small number of cases raise uncertainties about any such association.

Reproductive Outcomes: Military radar technicians have been the focus of most studies evaluating semen parameters and occupational exposure to RF.

The 2004 review of health effects associated with occupational exposure to RF included four cross-sectional studies of the effects of exposure to microwaves and radar among military populations on semen parameters.[2] Three of the studies found reductions in sperm density, with two showing decreases in sperm motility.[33-35] However, either the recruitment strategies were poorly described or there was a substantial non-response rate among these studies.

Grajewski and colleagues (2000)[14] conducted measurements at four plastic sealer (dielectric heater) worksites. Machines emitted frequencies between 12 and 57 MHz and electric field strength ranged from 1.1 to 3.0 V/m. No significant difference was seen between exposed and unexposed workers in sperm density, counts, motility and morphology. However, the study was likely underpowered, with only 12 exposed workers and 34 unexposed. All three reviews of occupational health studies[1-3] suggest further investigation of the effects of RF on fertility, given the known susceptibility of spermatogenesis to heating.

Cardiovascular disease: The possibility of increased risk of cardiovascular disease due to occupational exposure to RF was demonstrated in several early studies from the former Soviet Union. These primarily examined the acute adverse effects of microwave exposure on physiologic measures such as blood pressure and heart rate.[2] Studies of major clinical outcomes have failed to find an association. Three large retrospective cohort studies of American[28] and Belgian military personnel[5] and Motorola workers[30] did not find an increased risk of mortality from heart disease.

Cataracts: The lens of the eye is known to be sensitive to heat compared to other organs; however, epidemiological data linking RF to cataracts is limited. Two case-control studies of American military veterans, both published before 1980 (as cited in Ahlbom, 2004[2]), found no association between the presence of lens opacities and RF exposure from jobs using radar or microwaves. A 1984 Australian study of 53 radio and TV transmitter workers found an increase in prevalence of lens opacities (a precursor to cataracts) compared to 39 "non-radio linemen" from the same communication organization, with 18% prevalence in the transmitter workers compared to 8% in the control group (p-value of 0.043).[36] Antenna emitted frequencies ranged from 558 kHz to 527 MHz. There were no exposure limits for these workers until 1981, and measurements of power density around the work areas varied from 0.08 mW/cm^2 to an extremely high value of 3956 mW/cm^2. However, these studies did not take into account possible differences in exposure to solar radiation, a known risk factor for cataracts.

In summary, most of the epidemiological studies on the association of occupational exposure to RF cancer and cardiovascular disease mortality were negative, based on military cohorts exposed to radar. Exceptions were mixed findings for leukemia. Although there appeared to be an effect of occupational RF exposure on male semen, also in military populations, these results were dubious due to poor study methodology and reporting. The few studies on cataracts showed mixed results. All of these observational studies had problems of poor exposure ascertainment and other potential biases which would affect the outcome.

8.3.5 Discussion on occupational health risks from exposure to RF

Workers in a wide variety of industries are exposed to RF radiation of different frequencies and exposure levels. Current safety guidelines are based on preventing the established acute effects of tissue heating and RF shock. Long-term follow up of workers with acute overexposure may assist in determining whether there are any lasting effects of short duration high-level exposure to RF.

The health effects of chronic occupational exposure to RF have been evaluated in a few studies, but these are often subject to limitations in study design which affects the validity of their findings. The most common limitation is low power, due to the relatively small number of workers studied for relatively rare disease outcomes. Even with large cohort analyses, the quality of exposure assessment is a major limitation. Relying on job titles and lack of exposure measurements are generally a poor proxy of actual exposure. As a result, misclassification of exposure will reduce the statistical significance of a finding, indicating no effect. An additional complication for retrospective studies is that current exposure measurements may not apply to conditions in the past.

Recommendations for improving exposure assessment for prospective cohort studies have been put forward. Breckenkamp et al. (2009)[37] assessed data quality for 21 occupational cohort studies including airport workers, telecommunication technicians, and induction machine operators. Groups were evaluated using four criteria: duration and degree of RF

exposure, ease of individual exposure assessment, ability to assemble a cohort of sufficient size and means of follow up. Only three groups were considered viable for the assessment of the effects of long-term RF exposure on health: amateur radio operators, operators of short- and medium-wave transmitters, and RF plastic welders. Because one aspect of the assessment criteria was the size of the industry in Germany, their findings may not be completely transferable to the Canadian or North American context.

Prospective occupational cohort studies would be better suited for the analysis of occupational health effects from RF exposure if cost and technological factors could be addressed. Use of personal RF monitors would improve exposure assessment by taking into account actual exposure of individual workers, rather than potential exposure from a fixed RF source. The development of biological markers as an early indicator of long-term health consequences would reduce the time for follow-up.

Because workers are potentially exposed to higher levels of RF and for longer durations than the general population, occupational health studies may be better able to detect potential health effects. However, generalizability of findings to public exposure to RF remains limited for several reasons: 1) occupational sources of RF exposure, such as radar and industrial equipment, are rarely encountered by the general public and exposure levels are often higher and may involve thermal mechanisms, unlike the lower exposures from public RF sources; 2) workers tend to be healthier than the general population; as such, comparisons of outcomes in a SMR or SIR analyses would result in an underestimation of risk due to the "healthy worker effect"; 3) women are usually underrepresented, and retirees and children are excluded; 4) the effects of RF are highly dependent on frequencies within narrow ranges; industrial EMF applications often use lower frequencies of RF, which have greater penetration into the body; and 5) simultaneous exposures to ELF and other chemical, biological and physical hazards in the workplace are common, and their potential effects should be accounted for in the study design and analysis.

Outcomes of occupational health studies have focused on cancer, particularly brain and blood cancers. Other neurodegenerative diseases such as multiple sclerosis, dementia, and Parkinson's disease remain unexplored. Early disease manifestations of cellular dysfunction should also be considered; however, without an accepted biological mechanism for effects from RF, early manifestations are difficult to identify and measure.

Despite these limitations, further occupational health research has the potential to provide useful data to inform policy on RF exposure for specific occupational groups. Although there are a reasonable number of occupational RF exposure-based studies, there are few epidemiological studies and almost no recent ones evaluating health effects from RF exposure in the workplace. Prospective studies which follow occupational cohorts over time that are exposed to similar exposures and frequency ranges as the general public (such as broadcast workers), may be most informative for alerting the scientific community of possible effects on public health resulting from exposure to RF.

8.4 Appendix A

Current Canadian Occupational Safety Regulations and Standards

In British Columbia, WorkSafeBC is the regulatory authority for compliance with Occupational Health and Safety Regulations, Section 7, Radiation.[38] WorkSafeBC regulations state that the employer must ensure that a worker's exposure to non-ionizing radiation, including RF, must not exceed exposure limits specified for RF in Health Canada's Safety Code 6[23] and Safety Code 25.[39] Three exposure situations, as described in Appendix A, are addressed in guidelines that consider the following scenarios: (a) distances less than 20 cm from the emitting antenna as measured by the Specific Absorption Rate (SAR); (b) induced and contact current limits and (c) environmental exposure assessments in the far field and near field.

(a) At distances less than 20 cm from the emitting antenna: Specific Absorption Rate (SAR)

For a worker standing at a distance of less than 20 cm from the source, the exposure to electromagnetic fields is described in terms of Specific Absorption Rate (SAR), which is the amount of electromagnetic energy absorbed per unit mass of tissue expressed in units of Joules/Kg-sec or Watt/Kg.

SAR represents the degree of **thermal effects** for exposures taking place at distances less than 1 wavelength from the RF source. Thermal effects are predominant in the RF range of **100 kHz–6 GHz** but not significant below 100 kHz.

In summary, whenever a worker is exposed to RF fields at distances shorter than 20 cm in the frequency range 100 kHz–6 GHz, it is recommended to determine the values of the SAR to ensure that the limits of Table 1 below are not exceeded.

Table1. SAR exposure limits for controlled (+) environments

Parts of the body exposed	SAR Limit (W/kg)	Observation
Whole body exposure	0.4	The SAR averaged over the whole body mass.
Head, neck, and trunk	8	The spatial peak SAR for the head, neck and trunk, averaged over any one gram (g) of tissue*.
Limbs	20	The spatial peak SAR in the limbs as averaged over any 10 g of tissue*.

(+) controlled environment means occupational areas, accessible only to workers.

Note: In situations where the determination of SAR is not practical, the measurement of the electric field strength and the magnetic field strength are used as an alternative.

(b) Induced and contact current limits

To minimize the risks of shocks and burns due to induced and contact electric currents generated by electromagnetic fields, a set of limits as shown on Tables 2 and 3 are applied.

The measurement of induced and contact currents is necessary to ensure that the exposure of workers is within these limits.

Table 2. Induced and contact current limits for controlled environments

1 Frequency f (MHz)	2 RMS (*) Induced Current (mA) Through:		3 RMS Contact Current (mA) Hand Grip and Through Each Foot	4 Averaging Time
	Both Feet	Each Foot		
0.003–0.1	2000 f	1000 f	1000 f	1 second
0.1–110	200	100	100	minutes

Note: The frequency f is in MHz

(*) RMS means "root-mean-square." It represents the quadratic mean of time-varying quantities that can take positive or negative values (e.g., sinusoidal functions). For example, if n values I_1, I_2 ...In of the induced or contact current are recorded during a period of time, the *rms current* will be:

$$rms\ current = \sqrt{\frac{1}{n}(I_1^2 + I_2^2 + I_3^2 + \cdots . I_n^2)}$$

Table 3. Time-averaged induced and contact current limits for different exposure times for the frequency band 0.1–110 MHz, applicable to controlled environments

Exposure time	Time-averaged induced/contact current (rms) through each foot
≥ 6	100
5	110
4	123
3	141
2	173
1	245
0.5	346
≤ 0.5	350

(c) Environmental exposure assessments in the far field and near field

In the far field, plane wave conditions exist and the electric field strength **E**, the magnetic field strength **H**, and the power density **S** are related by the following equations,

$$E / H = 377, \quad S = E^2/377, \quad S = 377\ H^2$$

where the value **377** represents the **characteristic impedance of free space** in units of Ohms (Ω).

Therefore, in the far field, i.e., at a distance larger than 1 wavelength from the antenna, the measurement of only one of the Quantities **E, H, and S** is enough to obtain the other two.

However, in the near field where plane wave conditions do not exist, the equations above are not valid and power density measurements are meaningless. Therefore, both **E** and **H** must be measured separately in the near field.

The exposure limits for RF workers according to frequency are shown in Table 4.

Table 4. Exposure limits for controlled environments

1 Frequency (MHz)	2 Electric Field Strength rms (V/m)	3 Magnetic Field Strength; rms (A/m)	4 Power Density (W/m^2) [far field only]	5 Averaging Time (min)
0.003–1	600	4.9	--	6
1–10	$600/f$	$4.9/f$	--	6
10–30	60	$4.9/f$	--	6
30–300	60	0.163	10*	6
300–1 500	$3.54\ f^{0.5}$	$0.0094\ f^{0.5}$	$f/30$	6
1 500–15 000	137	0.364	50	6
15 000–150 000	137	0.364	50	$616\ 000 / f^{1.2}$
150 000–300 000	$0.354\ f^{0.5}$	$9.4 \times 10^{-4}\ f^{0.5}$	3.33×10^{-4} f	$616\ 000 / f^{1.2}$

* Power density limits are applicable at frequencies greater than 100 MHz.

Notes: Frequency, f, is in MHz; a power density of 10 W/m^2 is equivalent to 1 mW/cm^2; a magnetic field strength of 1 A/m corresponds to 1.257 microtesla (mT) or 12.57 milligauss (mG).

The occupational exposure limits to static magnetic fields are summarized in Table 5 below.[40]

Table 5: Exposure Limits for Controlled Environments

Exposure characteristics	Magnetic flux density B
Exposure of head and of trunk	2 Tesla = 2000 mT
Exposure of limbs	8 Tesla = 8000 mT

Protection of Workers Against RF Fields

The exposure of occupational workers to RF fields must be kept under the limits of Health Canada's RF safety guidelines.

In order to ensure a safe environment for workers around RF sources in the industry, the following rules should be followed:

- Potentially hazardous RF machines and appliances should be appropriately labeled with proper safety instructions.
- Controlled areas around RF sources must be clearly identified by appropriate signs.
- Areas where worker exposure to RF waves is suspected to reach or exceed the recommended limits should be surveyed to determine the existing exposure levels.
- Occupational workers should wear personal RF exposimeters (see description in Section 4) to record the RF exposure (W/m^2) during work in RF environments. RF Exposimeters should also have alarm settings (at exposure limits as in Table 4 or less) to prevent accidental exposures from occurring.

Special Precautionary Measures

Workers wearing implanted devices

Precautions should be taken to ensure that any worker wearing implanted metal and/or electro-medical devices is protected against undesirable effects (induced currents, thermal effects, signal interference) resulting from the presence of RF fields.

Pregnant workers/fetus

Pregnant workers in the RF industry must receive the same protection as the general public to ensure that the fetus will not be exposed to excessive levels of RF fields (i.e., less than 0.5˚C of temperature increase). Therefore, the exposure limits applicable to pregnant workers are the same as those for uncontrolled environments, as shown in Table 6[23] below.

Table 6. Exposure limits for uncontrolled (**) environments

1 Frequency (MHz)	2 Electric Field Strength rms (V/m)	3 Magnetic Field Strength; rms (A/m)	4 Power Density (W/m²)	5 Averaging Time (min)
0.003–1	280	42.19	--	6
1–10	280/*f*	2.19/*f*	--	6
10–30	28	2.19/*f*	--	6
30–300	28	0.073	2*	6
300–1500	1.585 $f^{0.5}$	0.0042 $f^{0.5}$	*f*/150	6
1500–15 000	61.4	0.163	10	6
15 000–150 000	61.4	0.163	10	616 000 / $f^{1.2}$
150 000–300 000	0.158 $f^{0.5}$	4.21x 10-4 $f^{0.5}$	6.67 10^{-5} f	616 000 / $f^{1.2}$

(**) uncontrolled environment means public areas.

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Section 9

Epidemiological Studies on the Risk of Head and Neck Tumours and Cancers Associated with the Use of Mobile Phones

Table of Contents

Summary

- In the general population, tumours of the head and neck (including brain tumours are relatively rare. Because of their rarity, in order to demonstrate the possible effects of mobile phone exposure on the occurrence of these tumours, cases must be identified from large populations and over many years. Because many of the studies have involved international collaboration, common classification of tumours and common assessment of mobile phone use is a challenge. Comparing results between studies is also challenging.

- Considerations in assessing epidemiological studies of cancer in humans related to exposure to mobile phones include the age group studied, the type of cell phone to which they were exposed, the intensity and duration of exposure and the location of cancer with respect to where the mobile phones were typically held.

- We identified 10 reviews of epidemiological studies published between 2007–2012 relating head and neck tumours to mobile phone exposure.

- No published reviews assessing the relationship of mobile phone exposure to tumours other than to tumours of the head and neck were identified and there were no reviews of tumours associated with exposure to radiofrequency (RF), other than that from mobile phones.

- The most consistent result from the reviews and original studies was of no relationship between long term use of mobile phones and meningiomas (tumours in tissue surrounding the brain and spinal cord) or of parotid tumours (salivary gland tumours).

- Most of the original studies cited in the reviews did not find an increased risk of head and neck tumours associated with long-term use of digital phones. The exceptions were principally from one academic research group that demonstrated increased risks of head tumours related to use of the older analog mobile phones, cordless phones, as well as digital phones.

- Many of the meta-analyses (combining study results) and a few of the original studies found increased risks of specific head tumours with longer term use of mobile phones (typically, at least 10 years since first use of mobile phones), along with recall of using mobile phones preferentially at the same side of the head as the tumour. The tumours implicated were gliomas (originating from glial cells which surround neurons and can be malignant) and acoustic neuromas (benign (non-cancerous) cranial nerve tumours).

- An extensive review of scientific studies by the IARC Working Group in May 2011 concluded that exposure to RF from wireless phones was "possibly carcinogenic to humans" (Group 2B).

- Evidence that there may be a higher risk of head tumours from long term use of mobile phones and concerns about the vulnerability of children has led to calls for further research.

9.1 Introduction

Can the widespread use of devices which emit radiofrequency fields (RF) cause cancer? Brain cancer is of particular concern since hand-held mobile phones and cordless phones are used in close proximity to the head, resulting in the highest near field exposure to the brain of all sources of RF. The only known environmental risk factor for malignant brain tumours (gliomas) is ionizing radiation[1], emitted from such sources as medical x-rays, which have the ability to penetrate cells and deliver high levels of energy to intra-cellular structures and damage DNA. Although RF is non-ionizing, there is concern that tumours may arise through biological mechanisms that do not directly damage DNA.

The carcinogenicity of RF was assessed in detail by a working group of 30 scientists from 14 counties at the International Agency for Research on Cancer (IARC) in May 2011. Their finding of limited evidence of an association of RF and head tumours in humans was based on positive associations found in some of the studies linking glioma and acoustic neuroma to RF exposure from mobile phones. As well, they cited limited evidence of malignancy in animals and weak evidence for endpoints relating to the mechanisms of carcinogenesis, such as genotoxicity and gene and protein expression, cell signalling and oxidative stress.[2] Overall, the IARC classification of RF was supported by the majority of the panel of scientists as Group 2B "possibly carcinogenic to humans."[3] An IARC monograph "Non-ionizing radiation, Part 2: Radiofrequency electromagnetic fields" (Volume 102; 421 pages) was recently released following completion of the toolkit.[4]

Prior to the May 2011 meeting, reports from the World Health Organization and the US National Cancer Institute had concluded that there was no conclusive or consistent evidence that RF emitted by mobile phones is associated with cancer risk.[5,6] According to the 2011 publication of the standing committee of the International Commission on Non-Ionizing Radiation Protection (ICNRP): "Although there remains much uncertainty, the trend in the accumulating evidence is increasingly against the hypothesis that mobile phone use can cause brain tumours in adults."[7]

What is the scientific evidence that supports (or refutes) that an association exists between exposure to RF and an elevated risk of cancer?

9.2 Purpose

The objective of this section is to assess the findings of recent reviews of the epidemiologic literature concerning the risk of brain tumours and cancers in relation to long term use of mobile phones.

9.3 Methods

A database search of epidemiological literature pertaining to cancer outcomes from exposure to RF was conducted for the five-year period 2007 to January 2012 using Ovid Medline, EBSCO and Google scholar. Search terms and keywords for "RF" or "radiofrequency radiation" or "mobile phones" or "cell phones" were combined with terms for "cancer" or "malignancy" or "tumours." Upon review of titles and abstracts, all systematic and narrative reviews for which the focus was the relationship of RF exposure with brain tumours or any type of cancer were included. Further hand searching for relevant reviews was done from bibliographies of the reviews obtained. Narrative reviews for which cancer outcomes were described in brief as one of many effects of exposure to RF were not included. Excluded were reviews or outcomes where types of brain tumours were not specified, but instead were grouped together. Reviews on animal studies and other biological effects also were excluded, as they are the subject of Section 6 on cellular and animal studies of RF. Relevant critiques of the scientific literature and specific epidemiological studies were included for illustrative purposes.

Meta-analysis is a statistical technique used to combine the results of selected original studies to obtain a summary statistic, typically a summary odds ratio (OR). The OR represents the odds that an outcome will occur given the exposure (RF), compared to the odds of the outcome occurring in the absence of that exposure. A statistically significant association is reflected in an odd ratio where the 95% confidence interval (CI) does not overlap with OR=1. Ideally, systematic reviews are preferred to narrative reviews by providing clear descriptions of the literature search process and criteria for selecting articles that could then be duplicated by others. Not all systematic reviews apply meta-analysis, particularly when studies differ substantially in research design. Conversely, the publication may provide results of a meta-analysis, but detailed information on the review process literature search and selection criteria is not given.

A tumour is an abnormal mass of tissue that may be benign (non-cancerous) or malignant (cancerous). In the general population, tumours of the head and neck (including brain tumours) are relatively rare. There are approximately 100 specific intracranial tumours including more than 50 neuroepithelial tumours, almost 40 meningeal tumours and more than 10 peripheral nerve tumours.[8] The head and neck tumours described in the reviews included: 1) gliomas, 2) meningiomas, 3) acoustic neuroma and 4) parotid (salivary) gland tumours.

1) Glioma is a broad category of neuroepithelial brain and spinal cord tumours that arise from glial cells that surround neurons. They comprise approximately 60% of all nervous system tumours. Approximately 77% of malignant brain tumours are gliomas. Subtypes of glioma, include astrocytoma, oligodendroglioma, ependymoma and glioblastoma multiforme (having the worst prognosis).[9]

Gliomas are classified as low grade (I or II) or high grade (II or IV), the latter being malignant.

2) Meningiomas are neoplasms arising from the meningeal tissue covering the brain and spinal cord. As they grow, meningiomas compress adjacent brain or spinal cord tissue. Most (over 97%) are benign tumours that are encapsulated.

3) Acoustic neuroma, also termed Vestibular Schwannoma, is a slow-growing benign intracranial primary tumour that arises from the Schwann cells which enfold the vestibulocochlear nerve (eighth cranial nerve leading from the brainstem to the inner ear).

4) Parotid cancer is a malignant neoplasm of the parotid gland (a type of salivary gland). Most parotid tumours (80%) are benign. The incidence of this rare cancer is increasing, but risk factors are unknown.[10]

Other cancers, including testicular cancer, leukemia, uveal melanoma, non-Hodgkin's lymphoma and pituitary adenoma have also been suggested as possibly having a relationship to exposure to RF.

9.4 Results

In order to demonstrate the possible effects of mobile phone exposure on the occurrence of head and neck cancers, cases must be identified from large populations and over many years. Because many of the studies require international collaboration, common classification of tumours and common assessment of mobile phone use is a challenge. Comparing results between studies is also challenging.

Considerations in assessing epidemiological studies of cancer in humans related to exposure to mobile phones include the age group studied, the type of cell phone to which they were exposed, the intensity and duration of exposure and the location of cancer with respect to where the mobile phones were typically held.

Tumours become evident years after the exposures which may initiate and promote them. It would be expected, therefore, that any increase in brain cancer attributed to exposure from mobile phones would occur after many years since their first use. Early studies on brain cancer risk from mobile phones compared cancer in "never" vs "ever" users. Doing so disregards cumulative exposure, based on duration and intensity of use. The primary focus of this section is long term use of mobile phones, which allows for a more appropriate assessment of period of time since first use.

9.4.1 Characteristics of reviews

In the five years since 2007, there have been 16 scientific review publications which evaluated the relationship between long term exposure to mobile phone RF and head and neck tumours (Table 1). No reviews of the literature were found for which the

focus was the relationship of RF to any cancer, other than brain cancer. The RF exposures of interest were from wireless phones, almost exclusively from mobile phones. Note that many of the reviews include some common original studies, and therefore the summary odds ratios are not necessarily independent.

Reviews were excluded where the outcome information was insufficient for the following reasons: a) the type of tumour could not be distinguished, for example "all brain tumours" doesn't distinguish differential RF effects on specific tumours;[11,12] b) there was no individual study odds ratios presented for a narrative[13] or c) a limited pooled analysis included only the one author's studies.[14] The studies chosen for review and meta-analysis by Khurana and colleagues in 2009[15] were exact duplicates of those presented by Hardell et al. (2009)[16] and therefore were not repeated in the tables by tumour type. Kan et al. (2008)[11]did present summary odds ratios for individual brain tumours for regular use of mobile phones vs. no use, but for the analysis of 10+ years of use all brain tumours were combined.

Table 1 below describes the characteristics of the 16 reviews and the rationale for excluding five of the reviews.

Table 1. Characteristics of reviews of studies assessing the association of use of mobile phones with head and neck tumours (N=narrative review; M=meta-analysis; S=systematic review)

Reference	Type of Review	Time Frame	# Studies Selected / Searched	Inclusion Criteria	Outcomes	Comments
Corle et al. (2012)[17]	N	2005–2010	15 / NA	NA	Gliomas	Compared Hardell & Interphone studies
Hardell et al. (2011)[14]	M	2002–2010	4 / 4	Hardell studies only	Malignant brain tumours	EXCLUDED – Pooled own case-control studies only
Levis et al. (2011)[18]	SM	2000–2010	30 / NA	Mobile phone use ≥ 10-yrs & laterality analysis	Glioma, head tumours	Also others' results on analog, digital and cordless phones
Ostrom et al. (2011)[19]	N	2000–2010	13 / NA	NA	Glioma, head tumours	Compared long-term and ever/never use & genome associations
Repacholi et al. (2012)[20]	SM	< Nov. 2010	8 / 96	All languages	Glioma, head & neck tumours	Applied quality criteria for narrative review
Alhbom et al. (2009)[21]	M	2000–2008	14 / NA	NA	Glioma, head & neck tumours	Evaluated methods
Hardell et al. (2009)[16]	M	2001–2008	12 / NA	Mobile phone use ≥ 10-yrs & laterality analysis	Glioma, head & neck tumours	
Khurana et al. (2009)[15]	SM	< Dec. 2008	10 / NA	Mobile phone use ≥ 10-yrs & laterality analysis	Glioma, head & neck tumours	NOT TABULATED as used same data as Hardell et al. (2009) review
Kundi (2009)[22]	N	1999–2008	25 / NA	NA	Head tumours	Included a meta-analysis of subset of studies
Morgan (2009)[23]	N	< Mar. 2009	5/ NA 11/ NA	NA	Gliomas, head & neck tumours	Presented early and later (interphone) studies & critique of methods
Han et al. (2009)[24]	S	2001–2008	12/NA	NA	Acoustic neuromas	

Reference	Type of Review	Time Frame	# Studies Selected / Searched	Inclusion Criteria	Outcomes	Comments
Myung et al. (2009)[12]	SM	1968-2008	28/463	Case-control studies with risk estimates	Tumours	EXCLUDED – Not specific for type of tumour
Croft et al. (2008)[13]	N	< 2007	14 / NA	English only	Head tumours	EXCLUDED – Not specific for type of brain tumour
Hardell et al. (2008)[25]	M	2001-2007	21 / NA	Excluded mortality studies	Glioma, head tumours	Compared by laterality
Kan et al. (2008)[11]	SM	< April 2006	10 / 48	Exclude case reports, animal studies, non brain tumours	Head tumours	EXCLUDED – Not specific for type of brain tumour for long term analysis
Hardell et al. (2007)[26]	N	2001-2006	28 / NA	Excluded mortality studies	Gliomas, head tumours	Also studied effects of cordless phones

As shown in Table 1, six of the reviews had a systematic review format, incorporating details of the search process, and the majority of reviews conducted a meta-analysis without providing the search criteria. Only three of the reviews provided information on the number of studies searched. The time frame for the search strategy was not mentioned in eight of the reviews; in these cases it was assumed to be the range of years of the tabulated studies. Most of the reviewed studies were initially published in 2000 or 2001. The end date of reviewed studies was usually one year prior to publication.

Except for the review by Hardell et al. (2007)[26] which also evaluated brain tumour effects from use of cordless phones, all of the reviews were of studies of mobile phones. For the most part, the term "mobile phones" was used in all reviews to indicated digital phones (commencing with 2nd generation mobile phones). Some of the individual studies specifically conducted analyses on use of older analog phones which had much higher RF power output (phone technology is discussed in Section 5 on Exposure Assessment). The highest levels of exposure to RF from mobile phones are in the "near field," approximately less than 5 cm from the head.

9.4.2 Review findings

Some of the reviews, chosen for their analysis of effects of long-term use of mobile phones on head and neck tumours, also presented results for ever versus never use of mobile phones, which is useful for comparison purposes (Table 2). Note that the summary statistics are not independent for comparison between reviews, as they are each derived from many of the same individual studies.

None of the reviews which had also presented meta-analyses of "ever versus never" use of mobile phones showed elevated summary ORs for the head tumours glioma, meningioma or acoustic neuroma attributable to ever having used mobile phones. Most summary odds ratios were close to the no effect value of OR=1. For meningioma, the majority of combined odds ratios were lower than one, implying a protective effect of use of mobile phones. Only one review[20] included a meta-analysis on parotid gland tumours, with seven studies yielding a combined risk estimate for ever use (versus never use) of mobile phones of OR 0.87, with a 95% confidence interval of 0.73 to 1.04.

Table 2. Summary odds ratios and 95% confidence intervals for the relationship of head tumours with ever use versus never use of mobile phones

Reference	# Studies Glioma	Summary OR (95% CI)	# Studies Meningioma	Summary OR (95% CI)	# Studies Acoustic Neuroma	Summary OR (95% CI)
Repacholi et al. (2012)[20]	8	1.07 (0.89–1.29)	6	0.93 (0.77–1.12)	10	1.05 (0.77–1.42)
Alhbom et al. (2009)[21]	16	1.0 (0.8–1.2)	14	0.9 (0.8–1.0)	15	1.0 (0.8–1.4)
Hardell et al. (2009)[16]	11	1.0 (0.9–1.1)	9	0.9 (0.8–0.9)	9	1.0 (0.8–1.1)
Hardell et al. (2008)[25]	10	0.9 (0.8–1.1)	7	0.8 (0.7–0.99)	9	0.9 (0.7–1.1)
Kan et al. (2008)[11]	NA	0.86 (0.7–1.5)	NA	0.64 (0.56–0.74)	NA	0.96 (0.83–1.10)

Analysis of length of time since first use of mobile phones of at least 10 years is more appropriate than analysis of ever having used mobile phones, when considering the period of time needed for development of head and neck tumours, as well as cumulative exposure. Tables 3a to 3d present analyses of the association of potentially higher exposures to RF due to longer term use of mobile phones or longer latency (time since first use) and/or ipsilateral use on four major types of brain tumours studied. Ipsilateral refers to recall of use of mobile phones at the same side of the head as the tumour. The summary risk estimate (odds ratio for case-control studies) was tabulated where available; otherwise the number of positive studies was given, along with their citations. The comparison group for the calculation of the risk estimates were subjects with minimal or no wireless phone use. Note that the particulars of the significant studies, such as the type of wireless phone and laterality, may differ according to which type of study analysis was included in the review.

Gliomas were the most common brain tumour studied, shown in Table 3a.

Table 3a. Findings on the association of long-term use of mobile phones with *GLIOMAS* in the reviews assessed

Reference	Long-Term Use	#Studies	Summary Risk Estimate*	Significant Studies
Corle et al. (2012)[17]	≥ 10 yrs	6 6	Increased risk of high grade gliomas in 2 studies No effect on low grade gliomas	Hardell et al. (2006a, 2006b)[27,28] of astrocytoma, digital and analog
Levis et al. (2011)[18]	≥ 10 yrs & ipsilateral	4	1.56 (1.21-2.00)	Hardell et al. (2008)[25] pooled analysis Lahkola et al. (2007)[29]
Ostrom et al.(2011)[19]	>2- to ≥10-yrs use	13	Increased risk in 1 study	Hardell et al. (2006b)[28] analog & digital on high grade astrocytomas
Repacholi et al.(2012)[20]	≥10 yrs or cumulative	5	1.40 (0.84-2.31)	Hardell et al. (2006b, 2010)[28,30] analog
Ahlbom et al. (2009)[21]	≥6 yrs	12	1.1 (0.8-1.4)	Hardell et al. (2006a, 2006b)[27,28] (pooled)) analog & digital
Hardell et al.(2009)[16]	≥10 yrs & ipsilateral	6 4	1.3 (1.1-1.6) 1.9 (1.4-2.4)	Lahkola et al. (2007)[29] Hardell et al. (2006b)[28] (for all glioma & high grade glioma)
Kundi (2009)[22]	>4 yrs & ipsilateral	9 3	Increased risk in 3 of 9 studies 1.5 (1.2-1.8)	Hepworth et al. (2006)[31] Lahkola et al. (2007)[29] Hardell et al. (2006b)[28]
Hardell et al. (2008)[25]	≥10 yrs & Ipsilateral	6 5	1.2 (0.8-1.9) 2.0 (1.2-3.4)	Hardell et al. (2006b)[28] (high grade and all gliomas) Lahkola et al. (2007)[29] (ipsilateral only)
Hardell et al. (2007)[26]	≥5 yrs & ipsilateral	8	Increased risk for 3 of 8 studies	Lahkola et al.(2007)[29] Auvinen et al. (2002)[32] Analog Hardell et al. (2006b)[28] also cordless

*A brief description is given when no summary risk estimate has been computed.

The number of studies included in each review on glioma ranged from 4 to 13, with exclusions due to short latency of use (less than 10 years) and/or contralateral phone exposure. In the most recent review,[17] distinction was made between an increased risk associated with high grade (malignant) glioma (as found in studies of astrocytomas by the Hardell group) and no effect found for low grade glioma. Significantly elevated summary ORs for head tumours related to long term use of mobile phones were shown in the review by Hardell and colleagues,[16] confirmed for ipsilateral use in a later review.[25] Reviews by Kundi et al.[22] and Levi et al.[18] also found an elevated summary risk estimate for glioma for ipsilateral exposure of at least 10 years' duration.

Original studies by Hardell and colleagues stand out by repeatedly demonstrating increased risks of brain tumours from wireless phone use, whereas most of the other primary studies from the reviews were negative. An exception was the positive findings by Lahkola and colleagues for risk of glioma (2005, 2006, 2007),[29,33,34] published as part of the INTERPHONE groups of studies. Differences in the number and choice of studies included in each review can be attributed, in part, to the time period covered and exclusion criteria. Arbitrariness in the choice of included studies is another consideration; for example, some reviews excluded the positive findings from Lahkola's studies.[29,33,34]

Each of the nine reviews on meningioma (Table 2b) included between 2 and 11 individual studies. None of the summary odds ratios from the reviews on the association of long-term use of mobile phones with meningioma were significantly elevated; the lower confidence limit for the pooled OR of 1.7 for ipsilateral exposure from Hardell et al.'s (2008)[25] review just missed statistical significance at 0.99. All of the positive individual studies were from Hardell et al.'s group, for which the risk was increased with use of analog (and not digital) mobile phones but also for cordless phones with greater than 10 years of use.

Table 3b. Findings on the association of long-term use of mobile phones with *MENINGIOMAS* in the reviews assessed

Reference	Long-Term Use	#Studies	Summary Risk Estimate*	Significant Studies
Levis et al. (2011)[18]	≥ 10 yrs & ipsilateral	3	1.27 (0.89–1.82)	All NS
Ostrom et al. (2011)[19]	>2 to ≥10 yrs	11	Increased risk in 1 study	Hardell et al. (2006b)[28] analog only
Repacholi et al. (2012)[20]	≥ 10 yrs or cumulative	2	1.25 (0.51–3.10)	Hardell et al. (2005)[35], analog Interphone study group(2010) – NS
Hardell et al. (2009)[16]	≥10-yrs use & ipsilateral	5 3	1.1 (0.8–1.4) 1.3 (0.9–1.8)	All studies NS
Kundi (2009)[22]	>5-yrs use & ipsilateral	9	Increased risk in 1 study	Hardell et al. (2005)[35] analog, ≥ 10-yrs use
Hardell et al. (2008)[25]	≥10-yrs use & ipsilateral	4 2	1.3 (0.9–1.8) 1.7 (0.99–3.1)	All studies NS All studies NS
Hardell et al. (2007)[26]	≥5-yrs use & ipsilateral	5	Increased risk in 1 study	Hardell et al. (2006b)[28] ≥ 10-yrs use of cordless phones (increased)

NS: Study risk estimates were not statistically significant (95% CI included "1")

*A brief description is given when no summary risk estimate has been computed.

The same nine reviews which evaluated meningioma also presented results (from 3 to 10 studies) on the risk of acoustic neuroma associated with long-term use of mobile phones (Table 2c). A consistent pattern was apparent in which the summary risk estimates for acoustic neuroma were elevated, particularly for ipsilateral exposure and longer duration of use. In addition to the original studies by Hardell and colleagues,[28,25,34,39] studies by Lonn et al. (2004)[36] of the INTERPHONE group, as well as Schoemaker et al. (2005),[37] supported findings of an increased risk of acoustic neuroma with ipsilateral exposure.

Table 3c. Findings on the association of long-term use of mobile phones with *ACOUSTIC NEUROMAS* in the reviews assessed

Reference	Exposure	#Studies	Summary Risk Estimate*	Significant Studies
Levis et al. (2011)[18]	≥10-yrs use & ipsilateral	3	1.73 (1.17–2.56)	Hardell et al. (2008)[25] Lonn et al.(2004)[36]
Ostrom et al. (2011)[19]	≥3- to ≥10-yrs use	9	Increased risk in 1 of 9 studies	Hardell et al. (2006b)[28] analog only
Repacholi et al. (2012)[20]	≥10-yrs use or cumulative	4	1.37 (0.74–2.52)	All NS
Hardell et al. (2009)[16]	≥10-yrs use & Ipsilateral	4 3	1.3 (0.97–1.9) 1.6 (1.1–2.4)	≥10 yrs and ipsilateral for Hardell et al. (2006b)[28] Lonn et al. (2004)[36] ipsilateral only
Kundi (2009)[22]	≥3-yrs use & Ipsilateral	6	Increased risk 3 of 6 studies	Lonn et al. (2004)[36] Hardell et al. (2005)[35] Schoemaker et al. (2005)[37]
Han et al. (2009)[24]	≥3-yrs use ipsilateral	12	Increased risk in 5 of 12 studies	Hardell et al. (2002,2005, 2008)[35,38,25] Lonn et al. (2004)[36] Schoemaker et al. (2005)[37]
Hardell et al. (2008)[25]	≥10-yrs use & ipsilateral	3	2.4 (1.1–5.3)	Hardell et al. (2006b)[28] Lonn et al. (2004)[36]
Hardell et al. (2007)[26]	≥3-yrs use & ipsilateral	7	Increased risk in 3 of 7 studies	Lonn et al. (2004)[36] Schoemaker et al. (2005)[37] Hardell et al. (2006b)[28]

NS: Study risk estimates were not statistically significant (95% CI included "1")

*A brief description is given when no summary risk estimate has been computed.

As shown in Table 3d, only two reviews presented data on the risk of parotid gland tumours from mobile phone use and both calculated a summary odds ratio of less than one (not statistically significant) for greater than 10 years of use. As was found for meningioma, Hardell et al.'s review (2009)[16] found an elevated but not statistically significant OR of 1.7 for ipsilateral use (the lower bound of the confidence interval was 0.96).

Table 3d. Findings on the association of long-term use of mobile phones with *PAROTID GLAND TUMOURS* in the reviews assessed

Reference	Exposure	# Studies	Summary Risk Estimate	Comments
Repacholi et al. (2012)[20]	≥10-yrs use or cumulative	5	0.83 (0.52–1.33)	All studies NS
Hardell et al. (2009)[16]	≥10-yrs use & ipsilateral	4 4	0.8 (0.5–1.4) 1.7 (0.96–2.9)	All studies NS

NS: Study risk estimates were not statistically significant (95% CI included "1")

There were no reviews which focussed on the relationship of RF to cancer outcomes, other than for brain tumours. The few narrative reviews which addressed this topic as part of a general review of health risks associated with exposure to RF did not present summary risk estimates on the few studies available.

9.4.3 Comparison of two reviews

Specific findings on glioma from two more recent review studies (having opposite conclusions) are described in Table 4a and 4b below.

A) *Repacholi MH, Lerchl A, Röösli M, Sienkiewicz Z, Auvinen A, Breckenkamp J, et al. Systematic review of wireless phone use and brain cancer and other head tumours. Bioelectromagnetics. 2012; 33(3);187-206.*[20]

Purpose: To conduct a systematic review to determine whether there is an increase in incidence of head tumours associated with use of wireless phones.

Methods: Five of eight studies selected evaluated long-term use of mobile phones (>6 years) on the risk of glioma, as shown in Table 4a. Data on analog rather than digital phones from Hardell et al.'s earlier studies were presented.

Results & Conclusion: A non-significant summary OR of 1.40 was found, with the greatest weighting from the INTERPHONE study. No consistent relationship was found between glioma or the other three head tumours and wireless phone use. There are insufficient data to make any determinations of the effect of longer-term use (>10 years) by adults.

Evaluation: Many of the European co-authors of Repacholi et al.'s review[20] have been involved in INTERPHONE studies. Although results for phone use were divided into short- and long-term use, there were no tables on ipsilateral exposure results. The 2006 study by Schuz et al. was a retrospective cohort study. Including a cohort study with case-control studies in a meta-analysis is not appropriate since the interpretation of a summary risk estimate relies on the assumption of common study design attributes in the combined data sets.

Table 4a. Results of studies selected by Repacholi and colleagues (2012)[20] on the risk of glioma from long-term use of mobile phones

Study First Author	Exposed Cases	Odds Ratio	95% Confidence Interval	Notes
Hardell et al. (2002)[38]	43	1.2	0.8–1.8	Analog phones Brain tumours
Hardell et al. (2006)[27]	48	3.5	2.0–6.4	Analog phones Brain tumours
Schuz et al. (2006)[39]	28	0.66	0.44–0.95	Cohort study on brain tumours Interphone collaborator
Interphone study group (2010)[40]	252	0.98	0.76–1.26	Multi-centre study
Hardell et al. (2010)[30]	38	2.4	1.4–4.1	Deceased subjects
Combined OR		1.40	0.84–2.31	

B) *Levis AG, Minicuci N, Ricci P, Gennaro V, Garbisa S. Mobile phones and head tumours. The discrepancies in cause-effect relationships in the epidemiological studies – how do they arise? Environ Health. 2011;10:59.*[18]

Purpose: A critical evaluation of publications concerning the association of mobile phones and head tumours was supplemented by a meta-analyses limited to subjects with ipsilateral tumours using mobile phones since, or for at least, 10 years.

Methods: Odds ratios were given separately for selected studies determining the risk of gliomas associated with long-term use of mobile phones (at least 10 years of use), with further restrictions to recalled ipsilateral exposures (Table 4b).

Results & Conclusion: The literature review and meta-analysis showed large and statistically significant increases in the risk of ipsilateral brain gliomas (summary OR 1.56, 95% CI 1.21–2.00) and as well for acoustic neuromas for subjects using mobile phones for at least 10 years.

Evaluation: All authors for the review were from Italian institutions and had no known affiliation with either the INTERPHONE or the Hardell group. Meta-analysis forest plot

results were given for data restricted to at least 10 years of latency, and contralateral and ipsilateral as well as combined results were shown. However, details on the data such as the size of the exposed sample were not readily apparent. Instead of using the combined INTERPHONE results, the smaller sample size of individual collaborator's data was used. The reference to Hardell et al. (2006) is a different study to that cited by Repacholi et al (2012). Bias in the recall of laterality could have affected the validity of the risk estimates.

Table 4b. Results of studies selected by Levis and colleagues (2011)[18] on the risk of glioma after ≥10 years since first use of mobile phones and with ipsilateral exposure

Study First Author	Exposed Cases	Odds Ratio (Ipsilateral)	95% Confidence Interval (Ipsilateral)	Notes
Lonn et al. (2005)[41]	25	1.60	0.80-3.40	Interphone collaborator
Hepworth et al. (2006)[31]	66	1.60	0.92-2.76	Interphone collaborator
Lahkola et al. (2007)[29]	77	1.39	1.01-1 .92	Interphone collaborator
Hardell et al. (2006)[28]	50	3.3	2.0-5.4	Astrocytomas: Analog & digital
Combined OR		1.56*	1.21-2.00	

9.5 Discussion

The findings of an increase in risk for glioma and acoustic neuroma after prolonged use and ipsilateral exposure from mobile phones (and perhaps cordless phones), as indicated in the combined analysis of original studies in many of the reviews, requires confirmation by further, more thorough research. Combining the results of individual studies allows for better power to determine an effect since many of the case-control studies are based on small numbers due to the rarity of tumours, and therefore the effect estimates have poor precision. However, the choice of study included in a meta-analysis is somewhat arbitrary, which results in differing summary estimates between reviews.

Acoustic neuroma is of particular interest as it grows within the skull where most of the RF energy from wireless phones is absorbed.[42] Nevertheless, given that many of the glioma tumours become malignant; these have a greater impact on health. The extensive review of epidemiological studies by the IARC Working Group which concluded that exposure to RF was "possibly carcinogenic to humans" was influenced by the positive associations of glioma and acoustic neuroma with longer-term exposure to RF from mobile phones found in a few epidemiological studies.[2]

Significant elevated risks were apparent only in two of the 10 studies of acoustic neuroma, with both studies from the Hardell group. Separate tables for case-control studies of the effects of longer term use of mobile phones and latency for development of tumours were not presented, yet there was a table of the two retrospective cohort studies which showed no effect on the incidence of glioma in males with long-term use (11–13 years).

The AGNIR report concluded that there was no evidence of an elevated risk of brain tumours within 15 years of mobile phone use, adding that data on longer latencies and long-term or heavy use of mobile phones were limited.

The most consistent negative findings from the recent reviews were for the relationship of exposure to mobile phones RF with meningioma and parotid tumours. The IARC Working Group concludes that the available evidence was insufficient to reach a conclusion concerning these two types of tumours.[2]

9.5.1 Cancers other than head and neck tumours

Reviews on health effects associated with exposure to RF stressed that there were methodological shortcomings in the few studies of non-CNS cancer and replication of the few positive studies either discounted the findings or have not been attempted.[43,44] The few studies available for leukaemia, lymphoma and other tumour types, including uveal melanoma (of the eye) and cancers of the testes, breast, lung and skin, were deemed by the IARC working group to be inconclusive due to methodological limitations and inconsistent findings.[2] Similar conclusions were given in the AGNIR report[45] which cited negative studies on testicular cancer and uveal melanoma (one study each) and in two studies of pituitary adenoma. Elevated risk estimates were found for leukemia associated with use of GSM mobile phones in one of three studies and for the less common T-cell lymphoma type of non-Hodgkin's lymphoma (one of two studies). The incidence of childhood leukemia has been associated with exposure to magnetic fields from Extremely Low Frequency (ELF) waves, but not specifically to RF.[25,43] Hardell and colleagues[46] found no overall increased risk for malignant melanoma in the head and neck region from use of wireless phones but recommend further study due to low subgroup numbers and methodological shortcomings inherent in a case-control study.

9.5.2 Case- control studies

Because brain tumours are quite rare, the most practical study design is a case-control approach in which cases (subjects diagnosed with specific tumours) are compared to controls, with exposures determined retrospectively, usually by interview or by questionnaire. The retrospective exposure assessment process is subject to biases, such as recall bias (due to differential recall of mobile phone use between cases and controls) and selection bias from low participation especially among controls.

In 1999, IARC initiated a large multi-centre case control study (the INTERPHONE study), involving 13 countries, to assess the potential risk of brain tumours associated with RF exposure due to mobile phone use. The resulting May 2010 publication described the analysis of a large number of subjects (2,708 cases of glioma and 2,409 cases of meningioma) diagnosed at ages 30 to 59 between 2000 and 2004 with comparable controls matched by age, sex and region of residence.[40] Key findings were a significantly reduced risk of both glioma and meningioma in regular users compared to non-users (including occasional use), no trend in risk with cumulative hours of use, but an increased risk of glioma 1.40 (95% CI 1.03–1.89) in the highest decile of recalled cumulative call time (>1640 hours of use). However, years of use or years since first use (> 10 years) were not related to risk. The researchers concluded that "biases and errors limit the strength of the conclusion we can draw from these analyses and prevent a causal interpretation."[47]

A number of methodological issues affect the quality of evidence from INTERPHONE and other case-control studies.[7,30,43,47,48]

1. A reduced risk implies a protective effect of mobile phone use, which is counterintuitive to expected effects, and may be a result of selection bias.
2. Misclassification of exposure may occur, for example, when the minimal requirement of "exposed" is using a mobile phone once a week for at least six months. Random errors would lead to underestimation of risk. Some systematic bias would result from underestimation of number of calls and overestimation of duration of calls, as demonstrated by validity studies.[8]
3. Differential recall of use of mobile phones by cases and controls is possible and prodromal symptoms (early symptoms associated with disease onset) among cases may reduce or stop their use of mobile phones.
4. A greater risk of reported ipsilateral than contralateral use is consistent with causation but also with bias if subjects over-reported use of the phone on the side of the head where the tumour was found.[49]
5. Most of the subjects are from metropolitan areas, yet exposures to RF are higher when mobile phones are used in rural areas (see Section 5).
6. A relatively short period of observation since first exposure to RF ignores the long induction and latency periods for cancer.[8] Defining the etiologically relevant period requires knowledge of the biological mechanism, which is currently unknown.

The major advantage of the INTERPHONE study was its size although the numbers were relatively small for the category of highest duration of use. The studies by Hardell and colleagues (discussed in 2011; 2010; 2009),[14,16,30] focussed on RF exposures after greater than 10 years of wireless phone use. The results of the smaller studies by the Hardell group usually differed from most studies in that the risk estimates obtained

were often increased for cases versus controls. The positive aspects of the Hardell studies included blinding to case status (avoiding observational bias) and better participation rates (reducing the possibility of selection bias) through use of mail questionnaires.[8,30] An analysis of methodological quality of 23 case-control studies on mobile phone use and tumours found the highest scores (8 of 9 possible points) for studies by Hardell and associates.[12] Replication of the results of the Hardell group by independent investigators would strengthen the credibility of their findings.

A unique aspect of the Hardell studies was including desktop cordless phones (Digital Cordless Telecommunications or DECT) as a source of RF (see Section 5). Long-term use of DECT resulted in elevated risks of specific brain tumours particularly with long duration of use and ipsilateral exposure.[14]

Children may potentially be at greater risk for adverse health outcomes resulting from exposure to RF. Vulnerability to the risk of brain tumours from mobile phone use is especially a concern due to the smaller distance to brain tissues and greater amount of marrow which increases transmission of RF.[50] According to Wiedemann and Schutz (2011),[51] there is no indication of an association between RF exposure and brain cancer in children, or for childhood leukemia. The few case-control studies generally have been negative[52,53] and are affected by limited power, bias and non-differential exposure misclassification (random error). A multi-centre international case control study of brain tumours involving approximately 2000 10–24 year olds (Mobi-Kids) is underway to investigate the role of RF exposures from mobile phones and other sources. However, according to Feychting (2011),[52] further case-control studies on children based on recall of past mobile phone use are unlikely to provide firm evidence, whereas monitoring of brain incidence trends in cancer registers are likely to provide the most robust evidence on potential effects of RF on the risk of brain tumours.

9.5.3 Cohort studies and incidence

To date there have been very few cohort studies designed to mitigate recall bias, selection bias and exposure misclassification. A recent retrospective cohort study by Frei and colleagues[54] found no evidence of increased risks of glioma and meningioma in just over 350,000 Danish mobile phone subscribers. While the problem of non-response and selection bias was avoided by using a computerized cohort and recall bias was not a factor with digitized subscriber data, exposure assessment was questionable, given that mobile phone subscription is not equivalent to actual mobile phone use (e.g. others, besides the subscriber may have use of the phone)[55] and information on length of call was not available. Similar limitations were apparent in a retrospective cohort study of acoustic neuroma, which concluded that there was no risk related to mobile phone use, determined by subscription to mobile phones.[56]

For all types of study designs, exposure assessment is a major problem, as accurate measurement of RF exposure is affected by technology used (see Section 5), use of hands-free devices, and the ubiquitous nature of EMF exposures from all sources. Large

prospective cohort designs, in which a cohort is followed over time, have the best potential for determining risks from exposure to RF. In this regard, a European multicentre prospective cohort study (COSMOS) was initiated in April 2010, which will follow 250,000 adult subjects over the next 20–30 years to assess the long-term health consequences of mobile phone usage, including cancer and neurological disorders.[42] Mobile phone use will be collected prospectively through questionnaires as well as network operator records.

Worldwide, there has generally been no increase in rates of brain cancer incidence in the last 20 years. For example, in the US between 1992 and 2006 the trends were downward or flat. The exception was for females aged 20–29 years, particularly for the frontal lobes which are less exposed to mobile phone RF.[57] The common belief is that a noticeable increase in the incidence of brain cancer should have occurred by now.[10] However Kundi (2011)[58] cite the long latencies of brain tumours and length of time needed to show an increase in incidence. According to Cardis and Sadetzki (2011),[59] a co-investigator with the INTERPHONE study, the identification of increased risks of solid tumours requires very long follow-up periods of subjects even with substantial exposure. For instance, no elevation in the risk of brain tumours was detected in survivors of Hiroshima and Nagasaki, Japan, for almost 40 years.

Close monitoring of national cancer registries remains an important endeavour to assess the potential for carcinogenicity associated with expanding use of multiple RF devices. In addition, there is a need to attempt to replicate positive study findings, increase study power and improve upon research designs, including better exposure assessment of RF from mobile phones and cordless phones, with consideration of technological changes.

9.5.4 Expert opinion on the IARC classification

Expert evaluation of the scientific literature regarding cancer risks associated with exposure to RF is ongoing. Quoted below are excerpts from statements by two well-respected international organizations in reaction to the classification of RF as a possible human carcinogen by the IARC Working Group in May 2011:

World Health Organization: "A large number of studies have been performed over the last two decades to assess whether mobile phones pose a potential health risk. To date, no adverse health effects have been established as being caused by mobile phone use.... WHO will conduct a formal risk assessment of all studied health outcomes from RF exposure by 2012."[5]

International Commission on Non- Ionizing Radiation Protection: "ICNIRP awaits with interest the full Monograph that explains the justification and arguments put forward by IARC in arriving at this conclusion. ICNIRP has been conducting a review of the potential health effects of RF including carcinogenicity as well as other aspects. The Commission will be publishing a revision of the ICNIRP guidelines on limiting RF exposure for the

general public and occupational groups. It will take into account all aspects of the literature including the material put forward in the IARC Monograph."[60]

9.5.5 Limitations of review

Due to the large number of epidemiological studies published on the association cancer from exposure to RF from wireless phones, this section was developed as a synthesis of reviews published in the past five years. As such, the results and discussion of each individual review may reflect biases of the authors. Heterogeneity of study inclusion and exclusion criteria was obvious from the different number and authorship of studies selected in each review. Some representative studies were selected more often in the different reviews, which would result in weighting of their study odds ratios to influence the overall summary risk estimates. However, use of specific criteria for choosing eligible studies in this section, the number of reviews included (ten), and the variety of review authors who were associated with either the international collaborative study INTERPHONE, Hardell's group of investigators, or were independent researchers, does support the representativeness of these findings with that of the scientific community.

9.5.6 Research gaps

A number of issues were apparent from the literature reviews and commentaries which emphasize the need for:

- More studies, not only of effects of RF exposure on brain tumours, but other cancers of interest; most of the positive studies that were repeatedly cited were published by one research group
- Improved research design and exposure assessment of case-control and retrospective cohort studies to minimize biases and random errors, and development of prospective cohort studies
- Applying knowledge of brain tumour latencies when defining case status in terms of a minimum period since first use of mobile phones.
- Validation of recall of ipsilateral versus contralateral use of mobile phones
- Evaluating effects of technology and use of hands-free options on exposure from different mobile phone devices (including smart phone uses) and also from cordless phones
- Assessing effects of multiple near-field and far-field exposures (i.e., WiFi, smart meters) to RF from different sources
- Assessing vulnerability to the effects of RF according to age group (including maternal exposures during pregnancy) and other personal factors.

9.6 Conclusion

Many of the reviews incorporating a meta-analysis, showed some evidence of an association of long-term exposure to RF (e.g., at least 10 years since first use) from mobile phones with gliomas and acoustic neuromas, especially with ipsilateral exposures (to the same side of the head as the tumour was found). This finding was not unanimous among the reviews and was observed mainly in the original studies of one group of researchers. Replication of these positive longer-term exposure studies by other research groups is needed to support suggestions of increased cancer risks from exposure to RF from mobile phones. Future research investigations must not only allow for longer latency times when determining the relationship of cancer to RF, but also apply more precise measurement of RF exposure taking into account the evolving and expanding use of RF devices.

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Section 10

Mobile Phones, Radiofrequency Waves, and Male Infertility

Table of Contents

Summary

- The purpose of this section is to synthesize pertinent research concerning the relationship between exposure to radiofrequency (RF) and effects on semen parameters and male infertility.
- Relevant publications on the epidemiology of reproductive effects from RF on human male in vivo and in vitro sperm studies, as well as selected animal research studies, were assessed. The literature was exclusively on exposure from mobile phones.
- Unlike the mixed findings found in occupational health studies of radar EMF exposures, the epidemiological studies of men assessed for infertility were consistent in demonstrating decreased sperm motility associated with increased use of mobile phones.
- In vitro laboratory studies, which involved exposing semen samples to controlled mobile phone RF exposure, generally noted a decrease in sperm motility, among other adverse effects. An exception was one study using purified, rather than unprocessed sperm, which lacks leukocytes and other factors important for sperm motility.
- While animal studies allow more control of the laboratory environment, the applicability of findings to humans is questionable. Studies of one type of rat (Wistar) tended to show adverse effects on semen parameters and implications of infertility associated with RF exposure, unlike those of Sprague-Dawley rats.
- Apart from the known thermal effects of RF, oxidative stress due to increased Reactive Oxygen Species (ROS) or decreased antioxidants is a plausible explanation for non-thermal effects of RF on sperm cells.
- Many of the epidemiological, in vitro and animal studies that were reviewed demonstrated biological effects on sperm motility related to RF exposure. Whether male fertility is impacted by RF is not yet clear. The positive findings highlighted here are unique among research endeavours examining possible health effects attributed to RF exposure and deserve more extensive research.

10.1 Introduction

Over the last 30 to 40 years, public concern over health effects related to RF has grown.[1,2] A specific concern is the possible effects of exposure to RF on fertility and viability of offspring.

Infertility affects about 15–20% of heterosexual couples of reproductive age, with half attributed to male factor infertility.[3-6] Often the amount of sperm produced is adequate, but the spermatozoa are functionally defective.[7] The quality of DNA carried within the sperm has been recognized as an additional factor in infertility.[8,9]

This section of the toolkit attempts to inform public health practitioners in their dialogue with decision makers and the public by providing a synthesis of pertinent research of the health effects of RF which may affect male infertility, and a summary of possible mechanisms for such effects. The majority of the literature on reproductive function describes the possible effects of RF on male sperm. The full spectrum of reproduction and development, including male sexual function and pregnancy outcomes such as spontaneous abortion and congenital malformations, as well as child development, will not be covered in the toolkit.

The purpose of this toolkit section is to assess current human and animal research into RF effects on sperm and male factor infertility.

10.2 Methods

Peer-reviewed papers from PubMed, Scopus, Ovid and Medline databases were searched from 2005 to 2011. Grey literature, including government documents, were also searched. The studies were limited to English. MeSH terms for radiofrequency radiation, male, fertility and infertility were among the keywords used and combined. Two recent reviews specific to male infertility and mobile phone RF exposure were used as a starting point in evaluating studies to include in this toolkit.[10,11] From the reference lists, abstracts were obtained where the titles were relevant to the subject of potential male infertility effects due to exposures to typical population levels of RF. Very few papers from the abstracts were excluded.

10.3 Results and Discussion

10.3.1 Human studies

Sperm cells are useful for the study of the cellular effects of RF as their characteristics are well known and the cells are easy to obtain. Human studies have been either retrospective observational studies, mainly on the extent of mobile phone use among men with infertility problems, or in vitro analyses of RF effects on human semen. Brief descriptions of the epidemiological and in vitro studies are given in Table 1 below.

Table 1. Human studies on the effects of exposure to RF on male semen parameters

Population	Methodology	Exposure	Endpoint Assessed	Results	Considerations
Fejes et al. (2005)[12] Is there a relationship between cell phone use and semen quality?					
371 infertility clinic patients, 30.8 ± 4.4 yrs	Retrospective; interview; self-report mobile phone use	Self-reported past cell phone use; 1. Low transmitter, <15 min/day 2. High, >60 min/day	Sperm concentration, motility	Decreased proportion of rapid progressive sperm motility with increased transmission time; increased slowly progressive sperm with increased transmission time	Self-report; unclear how duration of possession and use were assessed
Wdowiak et al. (2007)[13] Evaluation of the effect of using mobile phones on male fertility					
304 infertility clinic patients	Retrospective; questionnaire; self-report of GSM mobile phone use	Self-report of GSM mobile phone use 1. No use 2. 1-2 yrs sporadically used 3. >2 yrs regularly used	Sperm morphology, motility, concentration	Increased abnormal morphology with increased duration of phone use; decreased progressive motility with frequent phone use	No age range given; no significant differences between 3 study groups in terms of smoking, occupation, age, home region; different results according to "frequency" and "duration" of use but specifics unclear
Agarwal et al. (2008)[14] Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study					
361 infertility clinic patients, 31.81 ± 6.12 yrs	Retrospective observational; 4 groups stratified by self-recalled mobile phone use	Self-report of mobile phone use 1. No use 2. <2 hrs/day 3. 2-4 hrs/day 4. >4 hrs/day	Sperm count, motility, viability	Decreased sperm count, motility, viability, morphology, dependent on duration of daily exposure to mobile phone	Did not validate mobile phone use; did not classify type of phone; did not account for any confounders other than age; did not take other RF exposures into account

Population	Methodology	Exposure	Endpoint Assessed	Results	Considerations
Gutschi et al. (2011)[15] Impact of cell phone use on men's semen parameters					
2110 infertility clinic patients, 21.6 ± 6.6 yrs	Retrospective , recorded mobile phone use	Self-report mobile phone use (n=991) and non-use (n=1119)	Serum hormones, sperm count, motility morphology	Mobile phone users have increased pathological morphology (68.0% vs. 58.18%); lower % rapidly progressive motility (23.98% vs. 25.19%); higher free testosterone and lower luteinising hormone; all $p< 0.05$	Poor exposure ascertainment (no info on frequency, duration, placement of phone etc.) or other environmental confounders
Kilgallon and Simmons (2005)[16] Image content influences men's semen quality					
52 university students, 18–35 yrs	Experiment involving random allocation of explicit images; retrospective "lifestyle" survey	Self-report mobile phone use; explicit images viewed	Sperm motility, concentration	Lower sperm concentration and percentage motile sperm if mobile phone carried in hip pocket or belt	Only study that controlled for numerous "lifestyle" factors while assessing mobile phone use effect; not primary endpoint (intention of study) so details unclear
Erogul et al. (2006)[17] Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study					
27 healthy urology patients with normal semen parameters, 27 ± 3.2 yrs	In vitro; experimental split samples; neat ejaculate sample	GSM phone, 900 MHz, 2 W peak power, average power density 0.02 mW/cm^2 for 5 min, 10 cm away	Sperm motility	Decreased rapid motility; increased percentage of non-motile sperm; duration of possession and use negatively correlated with semen quality	Two observers per sample

Population	Methodology	Exposure	Endpoint Assessed	Results	Considerations
Agarwal et al. (2009)[18] Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study					
23 normal and 9 infertile patients	In vitro; neat ejaculate sample; exposed and control aliquots	GSM talk mode Sony Ericsson w3001 with AT&T 850 MHz, SAR 1.46 W/kg, max power <1 W for 1 hr, 2.5 cm away	Sperm motility, viability; reactive oxygen species ROS), total antioxidant capacity (TAC), ROS-TAC score; sperm DNA damage	Decreased sperm motility, viability, ROS-TAC; increased ROS; no difference TAC; no DNA damage	Age range unclear; didn't measure sample temperature; seminal leukocyte counts; may not mimic carrying the phone on belt / in pocket
De Iuliis et al. (2009)[19] Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro					
22 Normospermic 24.1 ± 1.1 yrs	In vitro; purified sperm; exposed and control aliquots	Waveguide function generator 1.8 GHz, SAR range 0.4–27.5 W/kg, 16 hrs	Sperm motility, vitality; ROS, oxidative stress; DNA damage	With increased SAR, there was decreased sperm motility, vitality; increased mitochondrial ROS and DNA fragments	Temperature was controlled; purified sperm samples were used
Falzone et al. (2008)[20] In vitro effect of pulsed 900 MHz GSM radiation on mitochondrial membrane potential and motility of human spermatozoa					
Semen samples from 12 subjects	In vitro; purified sperm; motility assessed by computer-assisted sperm analysis (CASA)	Signal generator; pulsed 900 MHz GSM-like RF at 2 or 5.7 W/kg, 1 hr	Mitochondrial membrane potential; sperm motility, kinematic parameters	Decreased sperm kinematic parameters straight line velocity (VSL) and beat-cross frequency (BCF) at 5.7 W/kg; no effect at lower SAR of 2 W/kg; no effect of mitochondrial membrane potential	Age range not clear
Falzone et al. (2011)[21] The effect of pulsed 900-MHz GSM mobile phone radiation on the acrosome reaction, head morphometry and zona binding of human spermatozoa					
12 samples from subjects aged 23 ± 5 yrs	In vitro; purified sperm; CASA	Signal generator; 900 MHz GSM-like, SAR 2 W/kg, 1 hr	Sperm morphology; acrosome reaction; sperm-oocyte interaction (binding)	Decreased competence to bind zona pellucida; no effect acrosome reaction	Flow cytometry cannot assess acrosome reaction stage, so an effect may not have been detected

10.3.2 Epidemiological studies

There have been a number of occupational health studies conducted on military and police exposed to radar devices, rather than mobile phone use.

Weyandt et al. (1996)[22] assessed exposures to microwave RF and aerosolized lead exposure in US military personnel from the Army Intelligence Corps and found that those with microwave exposures (assessed by duty assignment and questionnaire) had lower sperm counts. The same research group (Schrader, 1998)[23] later found no differences in sperm count or function. It was felt that exposure to intelligence radar in the first study would expose personnel to higher amounts of EMF than communication or missile tracking radar. Danish soldiers in another study on exposure to tracking radar with an estimated low maximal mean exposure of 0.01 mW/cm^2 had a non-significant reduction in sperm concentration.[24]

Fejes et al. (2005)[12] set out to conduct what they described as "the first human population study of the possible relationship between mobile phone use and semen quality." They enrolled 371 men who presented with infertility problems, assessing a number of aspects of mobile phone use including duration of possession, duration in standby mode when closer than 50 cm, and duration of daily use. Semen samples were collected by standard technique after five days of abstinence and analysed after liquefaction, according to standard WHO criteria for analysis and classification of sperm samples.[25]

Motility was assessed by percentage of sperm defined as rapid progressive (capable of penetrating the oocyte membrane), non-progressive (sperm which do not move forward) and immotile (dead); sperm count was done and analysis was repeated three weeks later with each subject providing a second sample under similar conditions. As with most studies investigating the cause of infertility, exclusion criteria for participants comprised behaviours and conditions known to affect sperm and semen quality including smoking, alcohol use, drug abuse, severe systemic illness or trauma within six weeks of the study, detectable organic alteration of reproductive organs or infection, and altered hormone levels of follicle stimulating hormone (FSH) and leutenizing hormone LH or testosterone. Of 611 consecutive men considered for inclusion, only 371 met inclusion criteria; all were Caucasian, ranged between 17–41 years with an average of 30.8 ± 4.4 years, and included a representation of a variety of social classes as assessed by level of education.[12]

As for assessment of RF exposure, low-transmitters were defined as those using a mobile phone less than 15 minutes per day; high transmitters, more than 60 minutes per day; short-standby, those who kept the phone in standby for less than one hour per day; and long-standby, for more than 20 hours per day.

It was found that duration of possession correlated negatively with the proportion of rapidly progressive sperm; the proportion of slowly progressive sperm also increased

with increasing daily transmission.[12] No significant findings were found between the long and short stand-by groups. Fejes et al. (2005)[12] concluded that there seems to be an adverse effect on sperm motility related to mobile phone use. They noted, however, that they did not account for a number of factors which influence potential RF effects from mobile phones, including the technology of the phone (e.g., pulse wave Global System for Mobile Communications (GSM) vs. continuous wave Code Division Multiple Access (CDMA)).[12,26] Further limitations were the inclusion only of men with presumed infertility who were enrolled due to seeking treatment, which may not be representative of the general population, and not considering other factors such as occupation.

Wdowiak et al. (2007)[13] studied the effect of mobile phone use on fertility in Polish men presenting for infertility assessment. They enrolled 304 men using three categories of exposure combining cumulative use and duration of use over time; 99 subjects did not use mobile phones, 157 had used GSM phones sporadically over 1–2 years, and 48 reported regular use for more than two years. Subjects answered a questionnaire and survey regarding phone use, and semen samples taken after 2–7 days of abstinence were evaluated according to WHO parameters. Exclusion criteria included those with varicocele, systemic illness, features of reproductive organ inflammation, BMI below 17 or above 30, and history of hormonal or reproductive development disorders. Questionnaires attempted to classify subjects by rural, town or city location (based on population size of residence,) amount of smoking, occupation, age and phone use. In evaluating the three subject groups, no significant differences in smoking, age, residence or occupation were found.

Concentration of sperm was classified into five groups according to the number of sperm cells in the ejaculate sample: severe; moderate; and light oligospermia (low concentration of sperm); and normospermia (normal sperm count and motility) respectively. Motility was assessed in four groups based on percentage of sperm in type A live forward progressive state. Morphology was assessed in five groups looking at percentage of normal sperm, with less than 3% being normal.

Using the above criteria, Wdowiak et al. found that 65.7% of men who did not use a mobile phone had a normal spermiogram, whereas only 35.4% of those using a phone regularly did.[13] Similarly those with no phone use had a greater percentage of sperm with normal morphology and motility; however, frequency of use according to the three exposure groups did not show a statistically significant association.

The researchers noted their results were congruent with those of other studies and concluded that the percentage of live progressively motile sperm of normal morphology decreased with frequency of GSM mobile phone use.[13] However, they failed to provide specific questionnaire questions or to validate the use of their questionnaire as an instrument to assess mobile phone exposure. Though they attempted to account for some confounding by asking subjects about occupation and smoking and

assessing differences between such groups, they failed to include other potential confounders such as alcohol use and other RF exposures. There was also no specific mention of age range of subjects, though it was stated that age did not make a significant difference in results.

In a prospective study of 13 men who used GSM mobile phones for six hours per day for one month, Agarwal et al. (2008)[14] evaluated sperm parameters in men undergoing investigation for infertility in an observational study. A total of 361 subjects were divided into those with no mobile phone use, those who used the phone for less than two hours per day, those using for two to four hours per day, and those with use more than four hours per day. In analysis using age as a covariate, it was found to be non-significant, which the authors interpreted to mean results were not biased by advanced age. Exclusion criteria were also similar to the previous studies, including smoking, chewing tobacco, alcohol use, male genital problems, tuberculosis, diabetes mellitus and hypertension. Samples were collected in standard fashion after five days of abstinence and analyzed according to WHO criteria.[27] The technicians analyzing the semen samples were blinded to the subjects' use of mobile phones.

Mean sperm motility, viability and normal morphology showed significant adverse effects in the mobile phone user groups, both in men with normal and abnormal sperm counts. A dose-response relationship was found as the assessed semen parameters declined with increasing mobile phone use, independent of the quality of the original sample.

Limitations for this study included data for type of phone and other variables known to influence RF exposure (e.g., occupation and other RF sources) not being collected. Age was the only covariate analyzed. Validation of mobile phone use was also not done, and Agarwal et al. relied only on subjective recall of history of use.[14] However, validation of mobile phone use has been performed for other studies and it has been found that subject recall is often reasonably adequate.[28,29]

The retrospective study by Gutschi et al. (2011)[15] was notable in that a large number of fertility clinic patients were included in the study. However, exposure ascertainment was crude, comparing those who used mobile phones to those who did not. With approximately 1000 subjects per group, even a small difference in sperm motility (23.9% for mobile phone users vs. 25.1% for non-users) was statistically significant ($p<0.01$), as were differences in morphology and serum-free testosterone and luteinizing hormone levels. Misclassification of the simple exposure variable of mobile phone use or not is likely. The authors admit to limitations in exposure ascertainment including no information on frequency and duration of use, whether the mobile phone was placed in pants pockets, or the influence of other environmental confounders such as occupational exposures. This study appears to be a secondary analysis since information on mobile phone use was "recorded" with no description given of a questionnaire or interview survey component.

A study by Kilgallon and Simmons (2005)[16] looking at the effect of type of image viewed on ejaculate parameters (not a study designed to assess the effects of RF), found that men who carried a mobile phone on a belt or in a hip pocket had lower sperm motility and lower sperm concentration according to WHO parameters (1999)[27] than those who did not carry a phone or those who carried a phone on a different body location.

This study recruited 52 heterosexual men aged 18–35 years old from the University of Western Australia and randomized them to look at sexually explicit images. Detailed questionnaires on lifestyle were filled out by participants, including questions on mobile phone use and the carrying position of mobile phones. While not looking specifically at the effects of mobile phones on semen quality, the authors concluded that even after control of all other lifestyle variables assessed by the study questionnaire, storage of a mobile phone near the testes (in a hip pocket or on a belt) had a significant negative impact on both sperm concentration and the percentage of motile sperm. As the study was not meant to address such associations, no information on mobile phone use (type of phone, duration of talk use, storage in on, off or stand-by mode, etc.) was provided, nor was exposure to other RF sources elicited. However, the study does seem to provide suggestive evidence of a relationship between proximity of mobile phone (worn on the hip pocket or belt) with semen quality.

10.3.3 Limitations of epidemiological studies

Although the studies included large enough numbers of men to have adequate study power, the populations were not broad enough to draw conclusions applicable to those outside the study population. Perhaps most limiting in population applications was the use only of infertile men as subjects, as well as the inclusion of predominately men of Caucasian/European origin. Thus the validity of applying results to the general male population is questionable.

As retrospective studies are, by definition, based on participant recall, assessment of mobile phone usage by study subjects is also uncertain. No study attempted to validate subject recall as a method of assessment of phone use, and so as a proxy of RF exposure. Further, few details were elicited or presented on specifics of exposure: how the phone was held; proximity to base stations (towers); type of phone; frequency; modality, etc. Specific duration (years of use) and accumulation of use (accumulation of minutes) was also vague.

While each retrospective observational study attempted to control for confounders first with exclusion criteria and then with analysis to assess significance between results when adjusting for confounders such as age, they were limited in their ability to do so. Although the data is compelling for an *association* between mobile phone use and altered sperm parameters, there is no evidence implicating mobile phone use as a *causative* factor. While one may be reasonably sure that among the Caucasian/

European men seeking treatment for infertility, self-reported mobile phone use was associated with alterations in semen quality (predominantly sperm motility), there is little clarity about a causative link, or accounting of confounding factors or even about the specifics of exposure relevant to effects on sperm function (type of phone, duration of use, etc.).

10.3.4 In vitro studies

Agarwal et al. (2009)[18] performed a small-scale prospective pilot study on unprocessed semen samples from 23 normal donors and nine infertile donors and assessed semen samples according to WHO parameters.[27] Semen samples were obtained by standard means after a period of abstinence of 48–72 hours, and after liquefaction, the samples were divided in half. One aliquot was exposed for one hour to a 850 MHz RF-pulsed mobile phone 2.5 cm away (having a maximal power <1 W and an estimated SAR of 1.45 W/kg). The phone's frequency was confirmed with an RF spectrum analyzer. The other half (control aliquot) was kept in identical conditions but was not exposed to the mobile phone. For control samples, power density was measured as being between 0.01 and 0.1 microwatt/cm^2 and the experimental samples, 2.5 cm from the phone antenna, were between 1 and 40 microwatt/cm^2.

Sperm motility and viability were negatively affected by exposure to RF. No significant differences in sperm concentration were found, nor was an alteration of DNA integrity observed in the experimental samples. Though room temperature was measured and controlled, sample temperature was not monitored. It is assumed that a mobile phone operating at such a low SAR (<2 W/kg) will negligibly increase temperature;[30,31] however, it is still prudent to measure.

Though this study was reasonably well controlled, blinding was not clearly explained in the paper, so it is unknown if technicians analyzing various semen parameters were aware of the purpose of the study or of which samples were considered experimental vs. control. While the distance from the semen sample to the phone was meant to mimic the distance between a phone carried in a pocket or on a belt, from the testes, it does not account for the clothing and tissue layers surrounding the testes in vivo.

De Iuliis et al. (2009)[19] also investigated the effect of RF exposure on human sperm from 22 normospermic donors, aged 24.1 ± 1.1 years old, a younger average age and more narrow distribution than many other studies. They liquefied the semen, which was then purified by separation of sperm from seminal plasma, with isolated sperms washed, centrifuged and then re-suspended. The sperm fraction of each sample was then analyzed for vitality, motility and cell density after the purification process and after experimental or control conditions.

Exposure was to RF of 1.8 GHz in the SAR range of mobile phones, (0.5–1.5 W/kg). A mobile phone was not used to create RF waves; rather a cylindrical waveguide was constructed that allowed RF at a frequency of 1.8 GHz to be propagated along Petri

dishes containing samples. SAR was measured in saline solution within and outside of the experimental system. Temperature of the same saline was also measured throughout the experiment as a measure of sample temperature, and was kept at 21˚C to avoid any thermal effects. Samples were exposed to SAR from 0.4–27.5 W/kg for a period of 16 hours, and all experiments were done at least in triplicate.

The investigators found a dose-dependent response for all tested parameters, including sperm motility and vitality. Decreased motility and increased levels of ROS were found in exposed specimens. The authors noted that in vitro studies are limited to approximately 24 hours of sperm viability due to limitations of culture media, and that sperm in vivo survived much longer during the one week transit time from seminiferous tubules to cauda epididymis, which would result in greater exposure to RF waves. As such, it is likely that a higher percentage of sperm may be adversely affected than indicated by this study, even if the presumably more susceptible ones were damaged first. The authors further noted another limitation of the culture media used, being inferior to epididymal plasma for sperm support, as would be found in vivo.[19] However, as a dose-response effect was found, it would seem there is biological and clinical relevance to their findings.

The study by De Iluiis et al. (2009)[19] is one of the best controlled in vitro studies of the effect of RF waves on sperm quality. Experimental parameters were strictly controlled and explained, and rationale for the frequency and SAR is logical and practical. However convincing though, the results were found on purified semen in vitro. Though the authors acknowledge this and point to previous studies supporting in vivo effects and effects on unprocessed samples, it is still difficult to translate this study to mobile phone effects on semen in "real life," and to link the effects observed with infertility.

Erogul et al. (2006)[17] have also looked at in vitro effects of RF waves on semen, in particular motility and concentration. They used a mobile phone to provide 900 MHz frequency, and assessed effect on semen collected from 27 healthy males.

Subjects averaged 27 ± 3.2 years and were recruited from patients visiting a urology clinic. Abstinence of two to seven days was required. Samples were split in half, one aliquot for control and one for experiment. The two groups of samples were rested at room temperature for 25 minutes and then separated; the experimental group was exposed to a GSM 900 MHz mobile phone, peak power 2 W, and average power density 0.02 mW/cm^2 for five minutes at a distance of 10 cm. Semen was analyzed after the rest period and 30 minutes after the exposure period in both experimental and control groups, at the same time, in order to reduce time-dependent motility variation. Analysis was done by two blinded observers; concentration and motility were evaluated through a counting chamber according to WHO criteria.

Significant differences between control and experimental groups were observed, including decreases in rapidly and slowly progressive sperm and increases in no-

motility sperm. No change was seen between groups in non-progressive motility or in concentration.

The authors assert that all environmental factors except for RF exposure were the same in each group, and so the noted change in motility can be explained only by the RF exposure. While the study does seem to be well controlled and conducted, it is mentioned that, despite blinding, inter-observer variability can occur in assessing motility on a qualitative basis, and that even by having two observers who are well trained, human error cannot be discounted.

Falzone et al. (2008)[20] focused specifically on sperm motility after exposure to pulsed 900 MHz RF. They noted that motility is a prerequisite for fertility, as sperm must journey to the ova and must be able to penetrate the zona pellucida. Due to the inherent inter-operator variability in manual semen sample assessment for WHO criteria, a computer assisted sperm analysis (CASA) was used.

Semen samples were collected from 12 healthy, non-smokers after two to three days of abstinence and kept at 37°C. Samples were allowed to liquefy for 30 minutes and parameters were evaluated and confirmed to be normal. Samples were then purified in three steps and the highly motile 95% layer was centrifuged and re-suspended. RF was produced by a signal generator and modulated with by a pulse duration of 0.577 ms with a repetition rate of 4.615 ms to mimic a GSM mobile phone system and administered using a waveguide. Temperature-controlled water was circulated through a 9 mm waterbed beneath the sample Petri dishes to allow control of a constant temperature.

Samples were exposed within the chamber to the 900 MHz GSM-like RF at either a SAR of 2.0 W/kg or 5.7 W/kg for one hour while controls were left beside the chamber for the same amount of time. Sperm were assessed after exposure, at two hours post-exposure and at 24 hours post-exposure. All tests were run in duplicate, and two samples were exposed and two kept as control. Using CASA, the sperm kinetic parameters evaluated were progressively motile sperm and parameters for velocity and frequency of movement. Progressive motility was not found to change significantly with either exposure, and no change in any of the velocity parameters was found with SAR 2.0 W/kg exposure. However, two parameters of motility, straight line velocity and beat-cross frequency, were significantly impaired after exposure to SAR of 5.7 W/kg.

Much criticism of in vitro studies of RF effects on sperm has focused on the influence of cofounders and the mechanism of observation, in particular lack of dosimetry (accurate measure of RF dose) and lack of automated semen analysis use.[32,33] Falzone et al. (2008)[20] attempted to address these concerns by carefully basing dosimetry on numeric simulations validated by temperature-based SAR measurement and carefully controlling the experimental conditions using a constructed chamber. Temperature effects were therefore not a consideration, as the chamber and temperature-controlled

water provided optimal temperature control. Use of CASA technology to assess sperm velocity and motion parameters negated observer bias.

In studies previously described, effect was found on rapid progressive sperm motility, in contrast to the negative findings by Falzone et al.[20] It is possible that the differing samples used (unprocessed vs. purified) is responsible for this by introducing leukocytes and their effects. It is also possible that manual assessment of motility was not as accurate and unbiased as use of CASA. In short, though Falzone et al. (2008)[20] did not find evidence of impaired sperm movement toward the egg (rapid progressive) as other authors did, they did find possible evidence of impaired sperm movement to penetrate the egg once there (hyperactivity).

Falzone et al. (2011)[21] continued their research on the fertility potential of sperm by examining the acrosome reaction, (release of enzymes from the anterior of the head of sperm when contacting the ovum, allowing for penetration and fertilization) head morphometry and zona pellucida binding ability (to protein membrane surrounding the oocyte plasma membrane) of sperm after exposure to 900 MHz of RF at SAR 2.0 W/kg for one hour, using methods similar to their 2008 experiments.

Acrosomal status was assessed at two and 24 hours post exposure, or control. Sperm-ooctye interaction was assessed using oocytes (immature egg cells) obtained from patients undergoing in vitro fertilization. Oocytes were thawed and bisected and the ooplasm was dislodged and kept at room temperature while experimental sperm were added to one half and control sperm not exposed to RF was added to the other. Binding capacity was determined by the ratio of sperm bound to the two halves, comparing the binding ability of the non-RF-exposed sperm to the RF-exposed sperm.

They found that there was no change in acrosome reaction even though morphometric parameters were altered with a significant reduction in sperm head area and acrosome percentage as well as decreased sperm-zona binding ability.[21]

Zona pellucida binding gives a good indication of fertility, therefore the finding of altered sperm binding to the zona pellucida after RF exposure implies an effect on male fertility. However, they caution that the in vitro effects noted should not be directly applied to in vivo situations and that much more research is needed to replicate the results and to explain the mechanism.

The previous studies addressed the relationship of semen parameters with exposure to RF from the use of mobile phones. An exception is the recent prospective in vitro study by Avendano et al. (2012)[34] involving Wi-Fi use in laptop computers. Semen samples from 29 healthy donors were divided into two aliquots incubated under identical conditions, but with one aliquot exposed in a separate room for four hours to a wireless internet-connected actively working laptop, 3 cm away from the specimen (to mimic the typical distance from a laptop placed on the lap to the testes). Laptop exposure induced a decrease in progressive sperm motility and an increase in the

percentage on non-motile sperm compared to unexposed controls ($p<0.05$). As well, sperm DNA fragmentation increased in the exposed group, allegedly through non-thermal effects (since the room and incubation temperatures, including laptop exposure, were kept constant at 25°C). The researchers concluded that the wireless use of a laptop computer positioned near the male testis may decrease human sperm quality, and with prolonged use there may be an impact on sperm fertility potential. At question was whether an active laptop without wireless internet connection would result in similar effects, which would imply a role of EMF exposure from the battery source.

10.3.5 Limitations of in vitro human studies

The in vitro studies on human semen attempt to address the limitations of epidemiological research. Most of the studies provided better control of exposure conditions, including specific frequency, SAR and power density exposure and more accurate dosimetry calculations. Varying degrees of blinding were attempted, and control samples were universally used. The effect of confounders, like proximity to an RF source, was adequately addressed. As with the epidemiological studies, it is difficult to compare results of the in vitro studies as the exposures and conditions evaluated were not consistent. Differences in use of unprocessed or purified semen and the practical use of evaluating isolated sperm instead of those in a more physiological state contribute to uncertainty in the effect of semen components on sperm motility. Differences in exposure to RF, in frequency, SAR, source and distance also make it difficult to compare results, as do differences in methods of evaluating effect, such as the use of computer assisted versus manual analysis.

Most, although not all studies attempting to control temperature, convincingly ruled out a thermal effect. Further, while one author acknowledged the effect of time on parameters under study, others did not attempt to consider the known effect of time since ejaculation affecting motility, resulting in a progressive decrease in the percentage of motile sperm over time. The human studies generally focused on sperm motility, which has plausibility as an important precursor to fertility; however, it is unknown what characteristics of exposure to RF may have impact on sperm motility. Although effects on sperm motility were found in the in vitro and epidemiological studies, whether these findings translate into “real world” decrements in fertility has yet to be convincingly demonstrated.

10.3.6 Animal studies

Although animal studies often provide more control of the experimental environment, the applicability of animal data to humans is always questionable. Characteristics and findings of the selection of animal studies are presented in Table 2 below.

Table 2. Animal studies on the effects of exposure to RF on male infertility

Subjects	Methodology	Exposure	Endpoint Assessed	Results	Considerations
Dasdag et al. (2003)[35] Whole body exposure of rats to microwaves emitted from a cell phone does not affect the testes					
16 Sprague-Dawley rats	Comparison of 2 groups, exposure and control	GSM phone Nokia 6110, 890–915 MHz peak power 2 W at 250 mW, SAR 0.52 W/kg, 20 min/day x 1 mo, 0.5 cm below cage	Testicular, epididymal lipid; malondialdehyde concentration; p53 immune reactivity; sperm count, morphology; histological structure of testes; rectal temperature	No effects	Low SAR postulated as the reason for no observed effects
Imai et al. (2011)[36] Effects on rat testis of 1.95-GHz W-CDMA for IMT-2000 cellular phones					
72 Sprague-Dawley rats, 5 wks old	Comparison of 3 groups; control, lower SAR, and higher SAR	CDMA phone, 1.95 GHz, SAR 0.4 or 0.08, 5 hrs/day x 5 wks	Testicular, epididymal, prostate weight; body weight; sperm count, morphology, motility; testicular histology; spermatogenic cycle	No effects	Used 5-wk old rats for 5 wks as period of sexual maturation is 5–10 wks
Yan et al. (2007)[37] Effects of cellular phone emission on sperm motility in rats					
16 Sprague-Dawley rats	Comparison of 2 groups exposure and control	CDMA phone, Nokia 3588i, 1.9 GHz trimode, SAR 1.8 W/kg, two 3-hr periods/day x 18 wks, 1 cm away	Epididymis sperm motility, morphology, count; mRNA for cell surface adhesion proteins; face temperature every 12 min; rectal temperature	Higher sperm cell death, abnormal clumping, decreased motility. Adhesion proteins up-regulated	Up-regulation of adhesion proteins associated with clumping: a possible mechanism for infertility?

Subjects	Methodology	Exposure	Endpoint Assessed	Results	Considerations
Dasdag et al. (1999)[38] Whole-body microwave exposure emitted by cellular phones and testicular function of rats					
18 Wistar rats	Comparison of 3 groups to RF (standby, speech, sham)	GSM phone, 890–915 MHz, 2 W max power; 0.141 W/kg, 1. Standby 2 hrs/day x 1 mo 2. Speech 3 x for 1 min over 2 hr/day x 1 mo 3. Control, 0.5 cm under cage	Left caudal epididymal sperm count; testicular histology; rectal temperature each week	Decreased epididymal sperm count in speech group (not statistically significant); decreased seminiferous tubule diameter in speech and standby group; elevated rectal temperature in speech group	Possible thermal effect as testes exposed in close proximity (0.5 cm) to phone
Kesari et al. (2010)[39] Mobile phone usage and male infertility in Wistar rats					
12 Wistar rats	Comparison of 2 groups, control and exposed	Mobile phone, 900 MHz, SAR 0.9 W/kg, 2 hrs/day x 5 wks	Protein kinase C; sperm count; sperm apoptosis; ROS	Decreased protein kinase C and sperm count; increased apoptosis and ROS	Relationship between ROS, PKC
Kesari et al. (2011)[40] Effects of radiofrequency electromagnetic wave exposure from cellular phones on the reproductive pattern in male Wistar rats					
12 Wistar rats	Comparison of 2 groups, control and exposed	GSM phone, 900 MHz, SAR 0.9 W/kg, 2 hrs/day x 5 wks	Antioxidant enzymes; malondialdehyde; histone kinase; micronuclei; reactive oxygen species; sperm cell cycle	Decreased glutathione peroxidise, superoxide dismutase (antioxidants), histone kinase; increased ROS, catalase, malondialdehyde; altered sperm cell cycle	
Mailankot et al. (2009)[41] Radio frequency electromagnetic radiation (RF-EMR) from GSM (0.9/1.8 GHz) mobile phones induces oxidative stress and reduces sperm motility in rats					
12 Wistar rats	Comparison of 2 groups, exposure and control (phone without battery)	GSM phone, 0.9–1.8 GHz, 1 hr/day x 28 days	Caudal epididymal sperm count, motility; glutathione; lipid peroxidation; facial temperature	Decreased sperm motility; increased lipid peroxidation, decreased glutathione in testis and epididymis; no change in sperm count; no temperature effects	

Subjects	Methodology	Exposure	Endpoint Assessed	Results	Considerations
Meo et al. (2011)[42] Hypospermatogenesis and spermatozoa maturation arrest in rats induced by mobile phone radiation					
40 Wistar rats	Comparison of 3 groups, control, exposure of 30 min or 60 min	GSM phone answer mode, 30 or 60 min/day x 3 mos, inside cage	Morphological changes in testes under light microscope	3 of 16 rats exposed for 60 min/day had hypospermatogenesis; another 3 had arrested maturation in testes; no effect was seen on the 16 rats exposed for 30 min/day	Do not specify RF exposure details
Ribeiro et al. (2007)[43] Effects of subchronic exposure to radio frequency from a conventional cellular telephone on testicular function in adult rats					
16 Wistar rats	Comparison of 2 groups, control and exposure	GSM phone, 1835–1850 MHz, 0.125 mW max average power, 1 W max peak power, 1 hr/day x 11 wks	Testicular and epididymal weight; lipid peroxidation; serum total testosterone; epididymal sperm count; seminiferous tubular diameter; rectal temperature	No effect	
Aitken et al. (2005)[44] Impact of radiofrequency electromagnetic radiation on DNA integrity in the male germline					
26 CD1 Swiss mice	Comparison of 2 groups to RF, exposure inside a waveguide and control (outside the waveguide)	3 GHz generator, 900 MHz, SAR 90 mW/kg, 12 hrs/day x 1 wk, cages inside waveguide	Sperm count, vitality and morphology; DNA strand breakage temperature; animal stress	No effect on sperm number, morphology; no DNA strand breaks; mitochondrial genome and nuclear beta-globin locus damage in epididymal sperm	~10x lower SAR than most other studies; no evidence of impact on germ cell development but possible evidence of genotoxicity

Dasdag et al. (2003)[35] continued their earlier research on mobile phone exposure effects on fertility using an animal model (Dasdag et al., 1999)[38] involving 16 Sprague-Dawley rats. Similar to their 1999 study, they exposed rats confined in plexiglass cages to RF waves. A Nokia 6110 GSM phone operating between 890 and 915 MHz, SAR 0.52 W/kg, average power 250 mW and peak power 2 W was placed 0.5 cm below the cage. Subject rats were exposed for 20 minutes per day to the phone in the "talk" position for one month. Control rats were exposed to a turned off phone.

Components measured included testicular lipid composition, malondialdehyde concentration (an index of sperm plasma membrane lipid peroxidation), and histological structure. The left caudal epididymis (where sperm is stored in the testes) was used to harvest semen to determine sperm count and morphology. Rectal temperature was measured to rule out thermal effects. No significant differences were noted in experimental and control groups; however, as there were only eight animals per group, the power of the study to detect significant differences was low.

The authors felt the low SAR accounted for the negative results, which are in contrast to those of a number of other older studies which showed adverse effects on seminiferous tubule epithelium, sperm count and morphology with exposure to high levels of SAR (30–44 W/kg) which themselves were enough to cause thermal effects.[45-47]

Yan et al. (2007)[37] did find adverse effects on sperm after exposing 16 Sprague-Dawley rats to a CDMA phone placed 1 cm away functioning at 1900 MHz, SAR 1.8 W/kg for two three-hour periods each day for 18 weeks.

They examined sperm from the proximal vas deferens (tube conveying sperm), and found that in the exposure group there was a higher cell death count, decreased motility and abnormal sperm clumping. In this study, the RF exposure time was longer, a different type of phone (CDMA instead of GSM) was used, and sperm from a different portion of the reproductive tract was assessed.

Using similar exposure (1950 MHz CDMA phone, SAR 0.04–0.08 W/kg), Imai et al. (2011) [36] examined the effect of RF on developing, five-week-old Sprague-Dawley rats, exposing them for five hours per day for five weeks. They did not find any difference in growth overall or testicular, epididymal (part of the spermatic duct system), or prostate weight. Further, no changes in sperm motility or morphology were found, and histology was normal

Overall, it does not seem that most studies support an adverse effect of RF on Sprague-Dawley rat semen or fertility potential. However, a number of recent studies on Wistar rats do seem to indicate a detrimental effect on sperm motility and, to a lesser extent, sperm count.

In 2011, Meo et al.[42] exposed 16 Wistar rats to one hour of RF each day for three months and found that a portion of the exposed rats showed hypospermatogenesis

(abnormally decreased production of sperm), and another portion had arrested maturation of sperm. Interestingly, the group of 16 rats the investigators had exposed to 30 minutes of RF per day for the same time course, showed no adverse effects, similar to the group of eight rats in the control group.

When Ribeiro et al. (2007)[43] exposed 16 Wistar rats to 11 weeks of GSM RF for an hour each day, they also observed no effects on the histological testicular parameters including testicular and epididymal weight, epididymal sperm count, seminiferous tubule diameter, and rectal temperature. This exposure time was chosen to include six seminiferous epithelium cycles, and so cover the period for spermatogonia to mature to sperm and reach the epididymis. By covering this time frame, they were confident they would detect change through all stages of development and so detect subtle effects if present.

In the study by Mailankot et al. (2009),[41] sperm motility was affected but not sperm count, after exposure of six Wistar rats to one hour of RF for 28 days from a GSM mobile phone.

The potential fertility effects of RF on other rodents (mice and rabbits) have also been investigated. However, not only is it difficult to compare results within a species, it is even more difficult to compare between species.

Aitken et al. (2005)[44] exposed 26 CD1 Swiss mice to GSM equivalent RF at 900 MHz, SAR 90 mW/kg for 12 hours per day for one week and did not find any effect on sperm morphology or motility.

10.3.7 Limitations of animal studies

There are obvious differences in the structure and physiology of the reproductive organs of animals and humans. The small size of the experimental animal means the effective exposure to RF is often greater. Though SAR and power density measures can be used to approximate what a person would be exposed to, it is difficult to be certain. The reproductive system also differs in size as well as in location and placement. A rat’s testicles for example are able to move freely through the inguinal canal, and so can migrate into the abdomen, altering the level of RF exposure during the experiment. The way in which animals are exposed also differs from humans; in many studies the animal is confined in a cage with the reproductive organs especially exposed to RF.

As with the human studies, it is difficult to compare results among animal studies. However there is often much better control of experimental conditions. Age, size and care of the animals must be considered. Most rats are kept in standard conditions, with free access to food and water, and are acclimatized to the experimental conditions (though for varying lengths of time) to minimize stress effects. Exposure parameters also differ, between animal experiments and between human ones. Source of RF

production, distance from animal, duration of exposure and intensity of exposure are not standardized. However, most authors have kept exposure parameters within those expected of a mobile phone, to rule out excessive RF exposure leading to possible heating effects.

10.3.8 Possible mechanisms

10.3.8.1 Thermal

It has long been established that thermal effects of RF waves may adversely affect human health, including male reproductive function. Short-term exposure to RF is known to increase testicular temperature and can alter seminiferous tubular epithelium (lining of cells in the testes area where sperm are produced).[45,46] However, exposure to RF from mobile phones has not been shown to generate enough heat to cause thermal effects. For example, even after six hours of mobile phone exposure, rectal temperatures were identical for the exposed and control rats, and therefore biological effects found were attributed to RF.[37]

10.3.8.2 Non-thermal

Though a number of different mechanisms have been proposed, increased oxidative stress (either from increased ROS or decreased antioxidant capacity) seems most likely to be implicated. It can explain observed effects on sperm directly and also indirectly through other possible mechanisms such as DNA damage.

10.3.8.3 Oxidative stress

Many of the effects noted on sperm after RF exposure seem to be related to increases in ROS which have a deleterious effect on sperm resulting in oxidative stress, which is a known factor in male infertility.[14,40,48-54] In 1992, Grundler et al. (1992)[55] showed that RF waves can induce ROS activity in cells.

RF has been shown to stimulate transmembrane NADH oxidase, an enzyme complex which transfers electrons from NADPH (a reduced form of NAD coenzyme) inside the cell across the membrane to be coupled to oxygen, which results in the production of ROS.[56] It is known that sperm have similar plasma membrane reduction-oxygenation (redox) systems, and so may produce increased ROS on RF exposure in a similar manner.[57-59] Mitochondria have been suggested as a source of ROS,[19] as have leukocytes found in semen outside of the sperm.[20]

Apart from inducing and increasing ROS, RF may also alter antioxidant enzymes, and so cause oxidative stress. Changes have been noted in erythroctyes (red blood cells)[60] as well as other tissues[35,38,43,61,62] when antioxidant enzymes have been assayed. However, it is unclear whether the RF is directly causing an effect on the enzymes or whether they are responding to a stress (even an oxidative stress due to increased ROS) effect. Non-enzyme antioxidants, like melatonin, have also been observed to

decline after RF exposure.[62-65] An additive effect may occur, with alteration not only of sperm cell enzymes but of whole body system antioxidants. Melatonin in particular is known to support antioxidant activity in sperm.[66] A number of recent studies have provided experimental evidence suggestive of an oxidative stress mechanism for the effect of RF on sperm.

Agarwal et al. (2009)[18] performed a small scale prospective pilot study on unprocessed semen samples from 23 normal donors and nine infertile donors assessing ROS, total antioxidant capacity (TAC) of seminal plasma, calculated ROS-TAC score and DNA damage by commercial kit. The TAC is the sum of enzymes and non-enzymes considered antioxidants and includes superoxide dismutase, catalase, glutathione peroxidise, ascorbate, urate, vitamin E, pyruvate, glutathione, taurine and hypotaurine. The score reflects the imbalance between ROS and TAC; a lower score is indicative of oxidative stress and infertility. They found that there was evidence for increased oxidative stress, as ROS increased with mobile phone exposure and ROS-TAC score decreased. Since sperm motility and viability were also decreased, the authors felt that induction of ROS and oxidative stress is a plausible mechanism for the deleterious effects seen on sperm exposed to mobile phone RF.

The authors provide a plausible explanation for the mechanism of action, stating that the increased ROS may be due to sperm plasma-membrane redox system stimulation by mobile phone generated RF.[18] However, they also note that an equally plausible mechanism would be an effect of leukocytes present in the unpurified ejaculate. Leukocytes are known to be involved in ROS production. They also note that some studies have found magnetic effects on ROS, and that magnetic fields in the present study were not examined.

De Iuliis et al. (2009)[19] also investigated the effect for RF exposure on human sperm with the hypothesis that oxidative stress is a common causative mechanism for disruption of sperm fertilizing potential and sperm DNA damage. The researchers exposed purified semen samples from 22 normospermic donors to RF frequency of 1.8 GHz with a SAR ranging from 0.4–27.5 W/kg. They performed standard measures of sperm motility and vitality, as well as ROS measurements and DNA damage assessments and all experiments were done at least in triplicate.

The investigators found a dose-dependent response for all tested parameters.[19] From 1 W/kg to 4.3 W/kg a significant increase in ROS was found and it was determined that the ROS were sourced from the sperms' mitochondria. At a SAR of 2.8 W/kg, the results became statistically significant for mitochondrially produced ROS. They noted specifically that rapid change occurred at low SAR exposures which reached a plateau when about 30% of sperm were affected. The researchers posit that even though they attempted to study only high quality purified sperm, a cohort of susceptible sperm exist which perhaps have abnormal, compromised mitochondria.

To confirm that the observed rise in ROS resulted in oxidative stress, expression of 8-hydroxy-2-deoxyguanosine (8-OH-dG), a marker of sperm DNA oxidative damage, was measured. An increase in expression was noted at lower SAR levels, which rose in a dose-dependent manner. A strong positive correlation between 8-OH-dG and MSP was found, indicating that the more ROS are produced, the higher the expression of 8-OH-dG, and so the higher the oxidative stress. An additional assay showed an increase in DNA-strand breakage from a SAR of 2.8 W/kg that increased in a dose-dependent manner and correlated strongly with ROS production and 8-OH-dG production.

The authors noted that in vitro studies are limited to approximately 24 hours of sperm viability due to limitations of culture media.[19] In vivo, sperm survive much longer during the one-week transit time from seminiferous tubules to be stored in the caudal epididymis, which would result in greater exposure to RF waves. As such, it is likely that a higher percentage of sperm may be adversely affected than indicated by this study, even if the presumably more susceptible ones were damaged first. The authors noted another limitation of the culture media used being inferior to epididymal plasma for sperm support, as would be the natural condition in vivo.[19] However, as a dose-response effect was found it, would seem there is biological and clinical relevance to their findings.

The study by De Iuliis et al. [19] is one of the best controlled in vitro studies of the effect of RF waves on sperm quality. Experimental parameters were strictly controlled and explained, and the rationale for the frequency and SAR is logical and practical. Results are internally consistent, and a plausible mechanism is explained based on ROS and oxidative stress. However, the results were found on purified semen in vitro. As such, it is difficult to translate the findings of this study to mobile phone effects on human semen in "real life," and to link such effects (if proven) with infertility.

Mailankot et al. (2009)[41] also looked at indications of oxidative stress in an animal study consisting of six Wistar rats exposed to RF from a GSM mobile phone. The mechanism to explain reduced sperm motility was suggested to be increased oxidative stress as indicated by increased lipid peroxidation (oxidative degradation of lipids) and decreased glutathione (an antioxidant).

Most recently, Kesari et al. (2011)[40] investigated the effect of RF from a GSM mobile phone (SAR of 0.6–0.9 W/kg) on oxidative stress in 12 Wistar rats exposed for two hours per day for five weeks. The mobile phone was placed on top of the cage instead of beneath, as was done by many other investigators. Experiments were done in duplicate in a blind pattern.

Glutathione peroxidise (GPx), catalase (CAT) and superoxide dismutase (SOD) were evaluated in sperm using an antioxidant kit with positive control, and it was found that both GPx and SOD decreased significantly in exposed animals, whereas CAT increased. Malondialdehyde (MDA), a reactive aldehyde known to cause toxic stress in cells, as well as ROS, and micronuclei formation were measured. Both MDA and ROS were

significantly increased in the exposed group, as were micronuclei. Given the increase in ROS and decrease in SOD and GPx (antioxidant enzymes), as well as the trends in MDA and micronuclei, Kesari et al.[40] concluded that the effect of RF was an enhancement of ROS, which likely led to increased lipid peroxidation and antioxidant enzyme alteration, and so oxidative damage. Given the alteration in the other parameters measured, such as increased micronuclei formation, an indication of DNA damage, an impact on fertility was felt likely.

Lack of support for a role of ROS in sperm effects was shown in the 2010 study by Falzone et al. in which exposure to RF had no effect on induction of DNA strand breaks or generation of ROS in purified sperm.[67]

Differences in studies of purified and unprocessed sperm (which have different compositions of mature and immature sperm) may also make sense in the context of an oxidative stress mechanism, as there is more potential for damage in an immature sperm than a mature one.[57] It would therefore follow that the unprocessed sperm in the study by Agarwal et al.[18] would show more effects than the purified, mature sperm in the study by Falzone et al.[20,67]

Overall, oxidative stress seems one of the more plausible mechanisms of RF-induced sperm damage. It has been found fairly consistently in human and animal studies on sperm specifically and on other cells in general. Mechanisms by which oxidative stress is caused by increased ROS and decreased antioxidant have been shown to exist in neurodegenerative diseases such as Parkinson's and Alzheimer's.

10.3.8.4 DNA damage

Increased production of ROS and increased oxidative stress have themselves, independently, been shown to damage DNA and other molecules, and DNA damage is known to be a factor in infertility.[10] However, studies on human lymphocytes have not shown DNA damage after exposure to mobile phone frequency RF for 24 hours.[68]

Although RF does not appear to have sufficient energy to damage DNA directly (as ionizing radiation may), other mechanisms of damage to DNA may be involved such as through ROS and oxidative stress, as well as up-regulation of gene expression and protein formation, including heat shock and adhesion proteins.[69-71]

Aitken et al. (2005)[44] exposed 26 CD1 Swiss mice to GSM equivalent RF at 900 MHz, SAR 90 mW/kg for 12 hours per day for one week and did not find any effect on sperm morphology or motility. Although they found significant damage to mitochondrial genes and the nuclear beta globin locu, no adverse effects on DNA strand breakage in sperm were noted.

As ROS can impact DNA, it is possible that RF may affect sperm quality through some forms of DNA damage, although the effects have not been as reproducible as ROS and oxidative stress effects.

10.3.8.5 Membrane potential and integrity

It is known that RF can induce currents in a cell membrane, and that this may alter the cation (positive ion) distribution (and so charge) in the normally negative membrane. Some evidence shows pulsed RF can dislodge calcium ions (Ca++) from a membrane, resulting in a weaker barrier and leakage, although there is no direct evidence on sperm membranes.[72] However, studies do seem to point to efflux of Ca++ as a factor in altered sperm motility.[51,65,72]

Studies have shown an effect on protein kinase C (PCK), and its alteration is implicated in altered sperm motility. As Ca acts as a secondary messenger, and PCK is one of its targets, this seems to implicate an efflux of Ca in decreased motility.[73]

For instance, Kesari et al. (2010)[39] found a significant decrease in protein kinase C (PKC) and sperm count in Wistar rats exposed to the same conditions described above. As PKC is known to be present in sperm and play a role in both motility and the acrosome reaction, these results point to a potential mechanism for deleterious effects of mobile phone RF on sperm motility and fertility potential.

10.3.8.6 Hormonal effects

RF effects on hormones and the pituitary gland have been studied to a much lesser degree than has sperm motility and morphology. Leydig cells in the testicle produce testosterone under the influence of LH, a hormone produced by the anterior pituitary. It is therefore plausible that alterations in testicular structures and in hormonal levels may be the causative mechanism for RF effects noted.

It is possible that oxidative stress and direct RF effects causing alteration in PKC, which is present in Leydig cells and seminiferous tubules, may explain altered Leydig histology in response to RF. One study showed that Leydig cells were especially sensitive to RF.[74] Alteration of testosterone receptors due to oxidative stress has also been implicated.[75]

There have also been studies showing no effect on hormone levels, testicular or anterior pituitary histology.[76-78] For example, when Ribeiro et al. (2007)[43] exposed 16 Wistar rats to 11 weeks of GSM RF for an hour each day, they observed no effects on total serum testosterone. An earlier study by De Seze et al. (1998)[79] looked at the hormonal effects in humans after exposure of 21 men to a 900 MHz mobile phone used for two hours per day, five days per week for five weeks. Because no effects on FSH, LH, GH, or PRL were noted,[72,80] the authors concluded that intermittent exposure to RF did not induce a cumulative effect on the hormone secretion rate of the pituitary gland.

A criticism of some of these studies is that the lower levels of RF exposure and shorter duration would be insufficient to assess the chronic effects of RF exposure.[64]

10.3.9 Limitations of studies on male infertility

The greatest limitation in evaluating the evidence on mobile phone RF and male infertility is the wide array of methods used to evaluate an even wider array of exposures.

Looking at studies to date, there is no consistency of RF source (phone or not, type of phone, mode of phone), location of RF source (distance, orientation), frequency, SAR, or power, although most investigators attempt to use a mobile phone or cell phone like RF, and so most studies are within 800–1800 MHz, SAR 0.04–<2 W/kg, and power <2 W.

In human epidemiological studies, reporting of mobile phone use is subject to misclassification of exposure. As well, there is no standardization of measuring duration of use in each instance (number of minutes per day) or of length of time of use (number of years since starting to use a mobile phone), nor of differentiating between talking on the phone, having the phone on and answerable, having the phone in standby or off mode, or of using a hands-free device with the phone. Texting, which has become an increasingly common use of mobile phones, has not been addressed, nor is use of other applications on smart phones. It is also difficult to find an ideal control group for human studies, as most people have been exposed to RF waves, and almost all have done so through personal mobile phone use. To complicate things, most people who are "light" users are older, further confounding the data. Few people are aware of previous RF exposures, and so it is difficult to account for them.

While animal studies have been better controlled and better reproduced than human studies, there are still discrepancies between species and between studies. Extrapolation of results to humans is also indirect and possibly irrelevant for some measured parameters.

While a plausible mechanism for fertility effects of RF exposure relating to oxidative stress and ROS has been postulated, the source and target of ROS remains unclear.

The rapidly changing nature of mobile phone technology also limits conclusions. Most studies were done on second generation pulsed GSM mobile phones which are being increasingly replaced by third and fourth generation continuous wave smart phones.

10.4 Conclusion

There is evidence of adverse effects on sperm with RF exposure, both in vitro and on the basis of epidemiological studies. The balance of evidence shows that human sperm exposed to RF exhibits decreased motility, abnormal morphology and increased oxidative stress. However, the number of caveats to the evidence, including the effects of confounders and unstandardized experimental designs, weakens the association considerably.

Almost all of the recent reviews on mobile phones and male fertility published since 2009 have concluded that sperm motility was the most consistent parameter showing a decline with exposure to RF.[11,18,81,82] The 2012 review by La Vignera et al.[11] further adds that sperm morphology is affected. Desai et al. (2009)[101] suggested a mechanism in which RF can stimulate extracellular superoxide production in semen, which would result in decreased sperm motility and viability. The detrimental effects of oxidative stress on sperm motility as well as semen parameters were emphasized by Hamada et al. (2011).[82] The review by Merhi (2012)[83] concluded that the evidence for RF exposure being associated with male infertility was weak due to diverse and inconsistent study conditions and stressed the need for further well-designed studies, as was recommended by all of the reviews.

To date, animal and human data are contradictory and difficult to evaluate due to heterogeneity of study designs including exposures, endpoints and intervening parameters measured. However, the balance of all evidence, animal and human, is consistent with the assertion that exposure of the testes to mobile phone RF may be associated with decreased sperm count, motility, concentration and altered morphology.

Evidence is less robust for decreased fertility; though it does follow logically, it is unproven that altered sperm parameters will adversely affect fertility, and it is unclear at what threshold of sperm parameters such an alteration of fertility would occur. Though sperm count and motility are accepted as measures of infertility, the rationale appears largely to be due to the simplicity of standardization and sampling.

Given that the balance of evidence is for some adverse effect, even if that effect cannot yet be precisely defined, it seems reasonable to proceed with caution. A recommendation is that short-term personal exposure for males be reduced by keeping mobile phones away from their genital area (i.e., not in pants pockets) and limiting mobile phone use. As industry is already moving to arguably safer use of RF in mobile phones, consumer encouragement may help this trend continue.

10.4.1 Gaps in the literature

Epidemiological studies ideally need to be conducted on larger, more heterogeneous populations, rather than limiting research to infertile groups. Studies should include men of all ages, as well as children and subjects going through puberty (though limitations on semen analysis must be considered). Diverse populations should be sought and compared, including race, geographic location, occupation, education and socioeconomic status. A potential study group would be healthy sperm bank donors. Control and adjustment of known confounders should be clearly documented, and consensus on what to consider as a confounder and how to adjust for it should be reached to facilitate study comparison. In this regard, stress effects are an important effect modifier of interest. The problem of finding a “control” population not exposed to mobile phone use may be addressed by careful comparison of duration of

possession, duration of use per day and type of use (i.e., texting, hand-free calling, storage of the phone and in which mode), as well as type of phone and network technology used.

Prospective studies are costly and time-consuming but with appropriate exposure assessment, limitations of bias and random error associated with retrospective observational studies could be avoided and allow more definitive evidence on the association of RF with male infertility.

There have been no studies on the effect of RF exposure to body organs from text messaging; there is also a lag in the study of newer technologies such as smart phones and fourth generation long-term evolution (LTE) devices.

In vitro studies must likewise strive to be comparable; agreement should be reached on the type of semen sample (unprocessed vs. purified, duration of abstinence) and the type of supporting media used. Conditions such as source of RF, proximity of source to sample, parameters of source (frequency, power, SAR, etc.) should be clearly defined. Endpoints should also be evaluated in a systematic, common fashion. Within individual studies, manual and automated analyses could be used, and samples should be run in duplicate or triplicate, and assessed by two observers.

Standardization of biochemical assays and preparation for testing would be helpful, as would clear justification of endpoints used as proxies to assess apoptosis, oxidative stress and other conditions. Use of the same sample for multiple analyses may be useful, but control for time elapsed and other alterations should be noted.

Animal studies may have more of a role in mechanistic determination and less in adverse effect confirmation due to the differences in reproductive anatomy and size. However, randomized controlled trials and true RF-naive controls will be an advantage of animal models. Again, studies should strive to be explicit with respect to experimental conditions and, if possible, similar to facilitate comparison. Stress effects and other confounding effects should be addressed and adjusted for. Consensus on semen location source (vas deferens vs. epididymis) and other easily altered parameters should be agreed upon or analyzed in each study.

Overall, a concerted effort would likely help in drawing more firm conclusions on the effect of mobile phone use on male infertility. Until then, conclusions should only be made within the limits of available knowledge, and should acknowledge said limitations.

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Section 11

Effects of Exposure to Radiofrequency Waves from Mobile Phones on Neurophysiology and Cognitive Performance

Table of Contents

Summary

- The question posed in this section is whether there is convincing evidence of non-cancerous effects on the brain from exposure to radiofrequency (RF) waves from mobile phones.
- All of the primary studies cited by the five reviews referenced has assessed the effects of RF exposures to the head from mobile phones. Mention was made in one review of three recent negative studies of base-station exposures.
- There is no evidence to date that exposure to RF from mobile phones has adverse effects on cognitive performance as measured by neurobehavioral tests of memory and attention.
- A consistent effect on brain physiology was of enhanced alpha brain wave activity.
- Among studies with positive effects, it was the pulsed modulation of second generation GSM mobile phone system that was associated with neurophysiologic changes.
- The positive results of some of the newer neurophysiologic techniques, such as measurement of increased brain glucose metabolism in the area of the brain near the RF-emitting antenna, suggest the possibility of subtle effects on brain physiology from exposure to RF, although the significance of such findings on behaviour or health is unclear.

11.1 Introduction

A major concern about exposure to RF is whether there are adverse effects on cognitive function. The highest personal exposures to RF are from mobile phones held to the head. Such symptoms as impaired concentration, tiredness, irritability and headache, are common complaints associated with exposure to sources of RF, as elicited through cross-sectional surveys.[1] Whether there is a physiological basis for these symptoms is unknown. Persons who suffer health problems attributed to exposure to RF are referred to as having "electrohypersensitivity" or "idiopathic environmental intolerance attributed to electromagnetic fields." This syndrome and studies of symptomatic complaints associated with RF are described in Section 12.

The perception and reporting of health symptoms is a subjective process. Although more objective invasive measurement techniques can be done on animals and using cell lines, it is problematic to extrapolate these findings to humans. Therefore only studies of human brain activity and cognitive performance ascertained through non-invasive physiological provocation techniques and neurobehavioral testing will be considered in this section. Provocation studies, which comprise an experimental (exposure) and sham (with no exposure) condition, ideally with double-blinding so neither the subject or investigator are aware of the exposure condition, are appropriate

for determining acute effects of RF fields. A discussion of biological effects, including results of animal studies are offered in Section 6. The focus of this section is to assess recent literature reviews concerning the effects of RF exposure on human neurophysiology and cognitive performance of healthy normal volunteers, with reference to representative studies.

Personal exposure to RF is highest for mobile phone use (see Section 5). As such, almost all of the studies on brain activity and behaviour are strictly on exposures from mobile phones. The question addressed is: "Is there convincing evidence of non-cancerous effects on the brain from exposure to RF from mobile phones?"

11.2 Methods

11.2.1 Article search strategy

Recently published scientific articles were searched through the OvidSP Medline database and with Google Scholar from 2009 to 2011. With Medline, the following search terms were used: electromagnetic fields/ radiowaves/ cellular phone/ microwaves, along with the keywords "radiofrequency," "radiation" and "EMF"; these were combined individually with the search terms: neurobehavioral manifestations/ cognition/ and keywords "cognitive function," "psychomotor performance" and "neurophysiological." Of 318 articles found, 267 remained when limits of "human" and "English" were applied; further limits to publication years 2009 to 2011 resulted in 28 scientific articles. After reading through titles and abstracts for review articles which presented an overview of mobile phone effects on human neurophysiology or cognitive performance, three published review articles were found (van Rongen et al., 2009[2]; Regel and Achermann, 2011[3]; Habash et al., 2009[4]), supplemented by Google Scholar search results of two additional review articles (Kwon and Hamalainen, 2011[5]; Valentini et al., 2010[6]). Findings from a condensed master's thesis (Brouwer, 2010[7]) was cited in the text. Illustrative study examples were chosen from the review reference lists and literature searches of more recent publications.

11.2.2 Included published review studies

A description of the characteristics of the five review studies which were published in peer-reviewed journals is given in Table 1.

Table 1. Selected general reviews on neurophysiological and/or neurobehaviorial effects associated with exposure to RF from mobile phones (2009–2011)

	Kwon & Hamalainen (2011)[5]	Regel & Achermann (2011)[3]	Valentini et al. (2010)[6]	Van Rongen et. al. (2009)[2]	Habash et al. (2009)[4]
Type of Review	Narrative with search strategy	Systematic	Systematic, with meta-analysis	Narrative	Narrative with search strategy
General Topic	Brain physiology & behaviour	Neuro-behavioral	Neuro-behavioral	Brain physiology & behaviour	Health effects in general
Databases	Pubmed & Web of Science	Pubmed & Web of Science	Medline + 9 databases	Not given	Pubmed, Embase, Medline
# Studies	105	41	42	Not given	Not given
Period	1997–2009	1998–2009	Not given	Not given	2004–2007
Conclusion on RF Effects	No effects or inconsistent findings	Inconsistent findings; no mechanism	No effects	Minor effects of GSM on physiology, but not behaviour	Small effects on physiology but no auditory effects

The review by Habash et al. (2009)[4] encompassed a broad range of health effects, including results of neurobehavioral and neurophysiology tests. Only one review, Valentini et al. (2001),[6] presented a meta-analysis including a forest plot of the common risk estimate of the relationship between RF and specific neurobehavioral tasks. This publication had the most detail of the review process, including over 8000 studies screened, but only one reviewer assessed the studies, whereas two reviewers are recommended for systematic reviews.[8] Other reviews relied on a narrative approach, including critique of the selected studies (particularly for the review by Regel and Achermann (2011)[3]. For three of the five published reviews,[2,3,6] no descriptions were given of the physiological or neurobehavioral tests undertaken (other than naming them) or the rationale for their use.

11.2.3 Interpretation of study validity

Study design is an important consideration as to whether the findings are valid and reproducible. Experimental provocation studies with a sham (no exposure) condition are best suited for evaluation of cognitive function. Provocation studies typically comprise one or more experimental conditions of a genuine RF field exposure (such as different levels of intensity) and a sham exposure. A crossover double-blinded design where subjects serve as their own controls and are randomly assigned to a specific exposure order (including sham exposure) is preferable. Double blinding, such that neither the subject nor the investigator is aware of the type of exposure applied, helps

to avoid bias. Adequate sample size is needed for good statistical power, which is the probability of detecting a change (at a selected probability level such as $p < 0.05$), given that a change has truly occurred.

For the majority of studies, exposures were from mobile phones with Global System for Mobile Communication (GSM) signals, typically having a frequency of 900 MHz with pulse modulated signals at 217 Hz. These systems have been widely used in second generation (2G) systems since the 1990s, and are still used in some of the third generation (3G) systems, particularly in Europe. A number of newer studies also evaluated the 3G Universal Mobile Telecommunications System (UMTS) introduced in the 2000s. It has a frequency of approximately 2100 MHz and uses the Code Division Multiple Access (CDMA) channel system which is characterized by a more continuous signal that is not pulsed (but with some amplitude variations at 1500 Hz due to adaptive power control).

Differences in exposure set up and dosimetry affect the amount of exposure of the cerebral cortex to RF.[3] Typically a modified commercial or generic mobile phone is used but there are differences between phone models and phone positioning (hand held or contacting the ear directly, right or left side of the head or both) and sometimes the only exposure is from the antenna. Carrier frequencies and pulse moderation affect the type of signal (e.g., GSM signals often use 900 Mz with 217 Hz pulse moderation). The strength of the field can be described as power in watts (W), power density (W/m^2) or specific absorption rate (SAR, the power absorbed per mass of tissue, measured in W/kg), which are difficult to compare. Relying on the peak SAR of the manufacturer does not give information on the degree to which the brain regions of interest are effectively exposed.

Often a single study involves the analysis of many different outcomes (and therefore testing of many hypotheses), particularly for neurobehavioral tasks. For example, if the probability against rejection of the null hypothesis is set at 5%, then one out of 20 comparisons could be significant on the basis of probability, when there is actually no statistically significant association between the studied variables. Whether or not to correct for multiple comparisons is controversial. According to Rothman, by adjusting for multiple comparisons (to reduce type I error, rejecting the null hypothesis of no effect), type 2 error is increased (accepting the null hypothesis, although the alternative hypothesis is true) leading to errors of interpretation and possibly missing important findings.[9]

11.3 Results

Findings from the recent reviews and examples of individual studies are organized according to “neurophysiology” (human brain activity) and “cognitive performance" ascertained through neurobehavioral testing.

11.3.1 Neurophysiology

11.3.1.1 EEG studies

A common method to evaluate human brain activity is by determining spontaneous base-line changes in electrical activity of the brain in the absence of a specific sensory stimulus through the application of electroencephalography (EEG), as recorded from electrodes positioned on the surface of the volunteer's scalp. Because there are wide variations between subjects in their EEG patterns, a crossover or "within-subject design" is necessary. Electrical activity occurring at the surface of the brain appears as waveforms of varying frequency and amplitude. Recording ongoing background activity of the brain is referred to as resting EEG, measured by calculating the power of each frequency band. Rhythmic brain activity is divided into different frequencies, consisting of the delta, theta, alpha, beta and gamma bands, which are bandwidths of increasing frequencies from <4 Hz (delta) to >30 Hz (gamma), obtained through spectral analysis of EEG signals. Most waves of 8 Hz and higher frequencies are normal findings in the EEG of an awake adult. Waves with a frequency of 7 Hz or less often are classified as abnormal in awake adults, although they normally can be seen in adults who are asleep. Sleep EEG is recorded continuously during sleep, using measurements of characteristic patterns of brain oscillatory activity for each phase of sleep. EEG waveforms of an appropriate frequency may be considered abnormal when they occur at an inappropriate scalp location or demonstrate irregularities in rhythm or amplitude.

The normal alpha rhythm has a frequency of 8–12 Hz and appears with eyes closed while relaxed. The alpha band is usually associated with cognitive inhibition and visual relaxation, including transition to sleep. Alpha activity disappears normally with attention (e.g., mental arithmetic, stress, opening eyes). Many of the studies on RF effects on EEG have been inconclusive. However, a relatively consistent finding from exposure to RF is enhanced alpha activity (at 8–12 Hz) in resting EEG, particularly in the older studies of 2G GSM exposures.[2,5] Enhanced spectral power (increased activity) in the alpha band in the sleep spindle frequency range (brain activity during stage 2 non-rapid eye movement sleep) has also been noted. No observed effect on resting EEG or during sleep has been found using 3G UMTS (non-pulsating) signals. While GSM signals resulted in minor effects on alpha and beta power during sleep, there was no effect on sleep latency, or any other indication of adverse health effects.[2] It was concluded by Habash and colleagues[4] in their update of the 1999 Royal Society of Canada report that, while there is some evidence to suggest that mobile phone RF exposure may lead to changes in brain activity, further research is needed to address study limitations and explore mechanisms underlying any effects.

This conclusion was supported by Marino and Carrubba[10] who undertook a thorough critical analysis of reports published prior to 2009 on RF effects on baseline EEG and on event-related potentials (a change in the EEG due to specific sensory or cognitive stimuli). They concluded that the question on the pathophysiology of mobile phone use

as reflected in brain electrical activity not only remains unanswered but unaddressed. In general, the 55 reports had attempted to study a nonlinear phenomenon using linear methods without proper controls while failing to consider experimental artefacts (a spike at the input occurs each time the stimulus is applied or removed) or the role of chance. Non-linear analysis was seldom applied, yet real effects can disappear due to averaging with linear analysis (such as ANOVA) as the stimuli produce both increases and decreases in brain alpha, for example. Almost all reports assumed incorrectly that the brain was in equilibrium with its surroundings and failed to distinguish low frequency EMF effects (from mobile phone batteries) from RF. Of the 55 reports on brain electrical activity, 48 were funded partly or in whole by the mobile phone industry.

Examples of EEG studies: An objective of the study by Kleinlogel and colleagues (2008)[11] was to investigate the effects of the new 3G UMTS technology on resting EEG.

Methods: The randomised crossover design with double-blinding involved 15 healthy male subjects (age range 20–35 years) being tested in a shielded room after fixation of EEG electrodes. The subjects were regular mobile phone users, without reported sensitivity to EMF and had normal hearing and vision and no history of major medial, neurological or psychiatric disorders nor head injury or substance abuse. Alcohol and mobile phone use were prohibited 12 hours before testing, while coffee and smoking were not allowed two hours prior.

After vigilance controlled resting EEG (eyes either closed or open while pressing the mouse key to a random tone) either the sham-exposure or the specific RF exposure was applied. RF signals were from an antenna, with either 2G GSM-exposure or 3G UMTS-exposure at weak (no modulation) and at high levels.

Results: There was no main effect of short-term exposure differences by type of exposure on vigilance control resting EEG (with frequency bands combined) before, at the start, at the end, or after exposure. The alpha1 band for the comparison of conditions was closest to being significantly lower at the start of exposure to the UMTS (weak) model (p=0.08). It was concluded that the study provided no evidence of short term effects of pulsed GSM 900 MHz or UMTS 1950 MHz EMF on resting EEG. The authors acknowledge limitations of small sample size, which allowed only strong effects to be detected and the pulsed test signal not conforming to that of a typical GSM-EMF mobile phone.

The study by Croft and colleagues (2010)[12] was the first to consider effects of RF on the EEG of different age groups.

Methods: The subjects were 41 adolescents (13–15 years of age), 42 young adults (the typical group studied, 19–40 years of age) and 20 older adults (55–70 years). All were healthy volunteers (those who were smokers, had substance abuse, hearing problems, head injuries, or history of personal or family psychiatric disorders were excluded). For 24 hours prior to testing, no alcohol or caffeinated beverages were to be consumed.

A double-blind, counterbalanced, crossover design (recommended for experimental human studies) was used, with each subject tested in a shielded room under Sham, 2G pulsed (GSM) and 3G (UMTS) conditions. Two cognitive tasks were undertaken with order counterbalanced across subjects either for an auditory oddball discrimination paradigm (responding to auditory stimuli that are dissimilar to the majority of auditory stimuli presented) or n-back test (indicating when the current stimulus matches the one from n steps earlier in the sequence), each followed by resting EEG, cessation of exposure, and a further resting EEG. The 2G exposure was through a Nokia 6110 mobile phone (using GSM technology) with the speaker removed to avoid audible sound and there was 50 dB background white noise generated. The 3G exposure was through use of a dummy model shaped like a typical mobile phone.

Results: Alpha power was greater in the 2G compared to Sham condition in the young adults (p=0.043). There was no increase in the 2G alpha power for adolescents (p=0.619) or older adults (p=0.47). For the 3G exposure compared to Sham, there was no main effect in adolescents (p=0.274), young adults (p=0.577) or older adults (p=0.557)). The authors concede that study limitations include low statistical power, given the small effect size. They concluded that the study supported the observation that effects on brain activity (alpha power) were more marked from the pulsed (2G) than the continuous (3G) RF exposures. However, it is unknown what the functional significance would be for an increase in alpha power in young adults.

Commentary on the studies by Kleinlogel et al. (2008)[11] and Croft et al. (2010)[12]: Both used appropriate experimental designs and included exposures from GSM and UMTS RF. Kleinlogel et al. included smokers (unlike Croft et al.) but purposely chose subjects without sensitivity to EMF. Combining the EEG bands for initial analysis does not allow any speculation as to physiological mechanisms since each band is associated with different properties. A further limitation of this study was not using actual mobile phones. Their version of the UMTS "weak" phone was found to affect the alpha1 band (of a narrower frequency range), unlike the more powerful UMTS "high" exposure model. This result puts into question the adequacy of the surrogate exposure. Prior to Bonferroni correction for multiple comparisons, this association would have been statistically significant and difficult not to emphasize. Croft et al. tested males and females but did not determine if there were sex differences and used less powerful non-parametric data analysis methods; however, the unique contribution of their study was demonstrating age group differences, as typically, studies use young adults only (such as Kleinlogel et al.'s). On balance, the study findings of Croft et al., which showed an increase in alpha power of young adults exposed to 2G RF, appeared to be more convincing.

11.3.1.2 Auditory and vestibular organ studies

The inner ear's receptor structures of auditory and vestibular organs absorb most of the radiation energy from the antenna of the mobile phone. The inner ear, being in

closest proximity to the mobile phone, would be expected to have a high absorption rate of RF leading to higher energy deposition in the cochlea. Findings of effects on otoacoustic emissions (sound signal generated from the cochlea to the outer hair cells) and auditory brainstem response (electrical response evoked from the brainstem by a sound stimulus) were mostly negative, based on short-term exposures to RF.[2,5]

Examples of Auditory Processing Studies: The aim of the study by Paglialonga and colleagues (2007)[13] was to assess subtle changes in cochlear function by measuring transiently evoked otoacoustic emissions (TEOAE, a standard validated method to determine cochlear outer hair cells functionality through measurement of dynamic changes) after exposure from GSM EMF signals.

Methods: Participants were 17 males and 12 females 23–30 years of age with no hearing disorders as determined by testing and questionnaire. A within-subjects double-blind study design was done, using a sham exposure and a commercially available GSM phone (NOKIA 6310) at 900 MHz and 1800 MHz. Using a phantom model, maximum SAR values of 0.41 and 0.19 W/kg were found for the 900 MHz and 1800 MHz frequencies respectively, which were much lower than the 2 W/kg limit.

Results: No significant differences were shown for the TEOAE parameters of mean energy and latency contrasting sham versus exposed conditions to a GSM mobile phone. Any observed changes in the parameters were suggested as random variation and not attributed to exposure.

Concern about possible auditory system effects of UMTS RF phones (as opposed to GSM mobile phones) was the basis for the study by Parazzini and colleagues (2009).[14]

Methods: Men (n=61) and women (n=73) 18–30 years of age had to have no evidence of hearing or hearing disorders based on testing and questionnaire responses, from which data was recorded using the ear with the best auditory results. Glasses and earrings were removed. A within-subject double-blind counterbalanced design was used. Auditory function measurements were in the following order:

- pure tone audiometry (PTA measures hearing threshold level, thus enabling the determination of the degree, type and configuration of hearing loss)
- auditory evoked potentials (AEP is a recording of brain electric voltage potentials from auditory frequent non-target and infrequent target stimuli)
- distortion product otoacoustic emission (DPOAE uses stimuli of two pure tones and two sound levels to record otoacoustic emissions that indicate cochlear or inner ear health)
- contralateral acoustic stimulation during transiently evoked otoacoustic emissions (CAS effect on TEOAE uses a brief acoustic click in the contralateral ear, allowing functional exploration of the auditory efferent system synapsing with the cochlear outer hair cells).

Speech at conversational level was delivered through an insert earphone (not through the mobile phone handset) to one ear and a UMTS mobile phone (Nokia 650) at another. SAR measurements made by phantom using the touch position of the phone, resulted in a level of 69 mW/kg for the 1947 MHz frequency of the UMTS phone at a 30 mm distance (approximately to the cochlea), which is well below the standard of 2 W/kg.

Results: After exposure to UMTS, the hearing threshold limit was increased particularly at 500 Hz (p=0.02) and at 2–8 Hz averages (p=0.03), but this was no longer statistically significant with statistical adjustment for multiple comparisons. The findings of all other audiometric tests showed no statistically significant differences and therefore there was a lack of corroboration. It was concluded that there were no general effects on the human central or peripheral auditory system due to short-term (20-minute) exposure of a UMTS phone. This study had an adequate sample size, supported by a priori sample calculations, and excellent protocols, similar to the previous study by the same authors on the possible effects of GSM phone signals on auditory function, which also concluded that there were no effects of RF on the audiological measures.

Commentary on the studies of Paglialonga et al. (2007)[13] and Parazzini et al. (2009)[14]: The study by Paglialonga and colleagues was the first to look at effects of exposure to RF on energy and latency of TEOAE. However, by only presenting one type of auditory test, there is no chance to simultaneously evaluate other tests of cochlear function. The sample size was small (n=29) and the exposure duration of 10 minutes was relatively short in duration. Despite applying two different frequencies of GSM, any differences in results were not presented. The authors were careful to assess whether the data was normally distributed and not skewed and applied appropriate transformations to each parameter and then used MANOVA, which is ideal for repeated measures designs with more than one dependent variable. However, the limited sample size (especially if 50% of the subjects had a different exposure to RF) puts into question whether this powerful type of analytical tool was appropriate; as well, no “F” statistic nor p-value was given. The study by Parazzini et al. presented an analysis of a number of tests of auditory function. The sample size was larger (n=127) and exposure duration was longer, at 20 minutes. A negative aspect is the statistical analysis. Unlike the findings of Paglialona et al., all measures were regarded as “approximately” normally distributed and therefore a simple paired t-test was used to compare the sham and exposure conditions for all outcomes. Because each subject only underwent a sham and exposure trial, this analysis is reasonable, however correlations between outcomes complicates the analysis. The Parazzini et al. study presents a more convincing demonstration of the lack of effect of UMTS RF on auditory function.

11.3.1.3 Studies of cerebral blood flow and volume

Positron emission tomography (PET) scans (nuclear imaging technique for producing 3D images of functional processing, including cerebral blood flow), magnetoencephalography (measurement of magnetic field, produced by brain

electrical activity) and transcranial magnetic stimulation (which induces weak electrical currents in the brain with rapidly changing magnetic fields) and near infrared spectroscopy (NIRS) (a noninvasive optical imaging technique which measures hemoglobin concentration changes in the brain and changes in regional cerebral blood volume) are among the newer neurophysiological techniques employed to assess the effect of mobile phones on brain physiology. However, these have shown mixed results (e.g., cerebral blood flow either increased and/or decreased in specific brain areas) and the positive findings (such as altered event-related magnetic fields, reduced short intracortical inhibition and increased intracortical facilitation) are difficult to interpret.[2,5] For instance, in a much publicized recent study by Volkow et al. (2011)[15] PET scans were used on subjects exposed to cellular phones with CDMA (G3) modulation. They concluded that: "In healthy participants and compared with no exposure, 50-minute mobile phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This finding is of unknown clinical significance."

Examples of PET studies: The purpose of the study by Aalto and colleagues (2006),[16] was to determine the main effects of RF on regional cerebral blood flow (rCBF) using positron emission tomography (PET) imagery.

Methods: Healthy right-handed male volunteers (n=12) abstained from caffeine, nicotine and alcohol for 24 hours prior to the study, and from mobile phone use that day. An MRI was undertaken to exclude those with brain structural abnormalities. A double-blind counterbalanced within-subject design was conducted with subjects performing a simple neurobehavioral (memory) task during the PET scans and sham conditions. The 1-back memory task involved responding to a "yes" key to a particular letter on the computer screen (if it was the same as the previous letter); otherwise the "no" key was pressed. A factory model GSM phone was used with both the loudspeaker and battery removed, as previously it was noted that even subliminal noise might induce a change in rCBF in the auditory cortex. The subject also had an earplug in the left ear to avoid noise from the operation of the phone. The SAR measurements, using a phantom was 0.743 W/kg for 10 g tissue, with an extrapolated peak value of 1.51 W/kg.

Results: A decrease in rCBF was found during RF exposure at the site of peak EMF in the brain, while an increase in rCBF was seen in other lobes of the brain. The RF had no effects on reaction times (p=0.56) or accuracy of responses (P=0.37). The authors speculated that frontal cortex changes in rCBF may reflect changes in neuronal activity but would not be related to facilitation in cognitive performance. They conclude that "our results do not provide any evidence to suggest that use of mobile phones would be more harmful to brain tissue than normal cognition, which is also always accompanied by intense temporary changes in neural activity and rCBF."

The aim of the study by Volkow and colleagues (2011)[15] was to determine whether acute mobile phone exposure affects brain glucose metabolism, measured by using PET with

injection of fluorodeoxyglucose (FDG). The rationale is that brain glucose activity is a better marker of neuronal activity than using PET alone to measure cerebral blood flow.

Methods: Analysis was done on 47 healthy paid volunteers screened for absence of medical, psychiatric or neurologic diseases or addiction. Urine testing confirmed no psychoactive drug use. The within-subject crossover randomized design was blinded only for the subjects. FDG uptake was through sampling of arterial blood. Two mobile phones (Samsung model SCH-U310 mobile phones with code division multiple access modulation, 3G, were used). Exposure from the right mobile phone was started 20 minutes prior to FDG injection and maintained 30 minutes after. The mobile phones were then removed and participants underwent emission and transmission PET scans using whole body tomography.

Results: Whole-brain glucose metabolism showed no differences in glucose metabolism, however there were significant regional effects. In the region closest to the cellular phone antenna, there was an increase in glucose metabolism and no decreases were noted. They concluded that the human brain is sensitive to the effects of RF from acute mobile phone exposure and brain absorption of RF may enhance the excitability of brain tissue in regions close to the antenna, as measured by increases in glucose metabolism.

Commentary on the studies by Aalto et al. (2006)[16] and Volkow et al. (2011)[15]: Both studies evaluated subtle acute effects of mobile phone RF on brain physiology. In the study by Aalto et al., double blinding was used and scans were taken during the EMF or sham modes, all done while a simple memory task was used to minimize random variation in rCBF. In addition, they set out to determine if the physiological measures were associated with task performance (they were not). The results were inconclusive in that both decreases and increases in rCBF were found, similar to what would be seen in normal cognition. On the other hand, the 2011 study by Volkow et al. used FDG to evaluate glucose metabolism as a more direct and longer lasting indicator of brain activity. Negative aspects were not calculating SAR using phantom modelling, but just reporting the model specifications and not removing the phone battery, as done by the Aalto study. PET measurements were done after exposure, and not during. However, the results were more consistent with all measurements showing increased glucose metabolism when exposed to RF from the cellular phone.

11.3.2 Neurobehavioral testing

Neurobehavioral tests typically are non-invasive computer administered tests used to describe cognitive function constructs such as “attention” and “working memory.” Tests of attention require vigilance and focus when responding to changing visual presentations, while tests of memory require short-term recall of a previous visual presentation. As with neurophysiological studies, there are mixed findings on cognitive performance measures attributed to exposure to RF. Regel and Achermann[3] conducted a systematic review of 41 provocation studies (1998–2009) on mobile phone exposures between 1998 and 2009. For over one half of the studies concerning exposure to mobile

phone RF, no behavioural changes were found; six of the studies noted improvements in performance speed, whereas seven showed decreases in performance. Accuracy of performing the test was worse in two studies, but improved in four studies.

According to Valentini and colleagues[6] it is only the tasks involving reaction time that appear to be affected by RF exposure, but this finding was weak, with the more recent studies showing negative outcomes when attempting replication of previous positive results or applying stricter statistical methods. They cited a previous meta-analysis[17] which showed the most consistent finding to be decreases in reaction time (improved performance) in a subtraction task.

There were no significant effects of 3G UMTS signals in any of the cognitive performance tasks as reviewed by Kwon and colleagues.[5] As well, Valentini et al.[6] did not find positive studies of neurobehavioral effects with longer-term exposure to RF such as testing with two-hour daily exposure over three weeks. In general, studies of cognitive function have generally found no correspondence between cognitive performance and changes in neurophysiological parameters.

All studies focused on RF exposure from actual or constructed mobile phones, with the exception of Kwon et al. (2011),[5] who cited three recent studies of base station-like exposure (far-field RF). Exposures to RF fields from base stations are usually much lower than exposures from mobile phones. These studies fulfilled basic inclusion criteria of having controlled exposures, being double blinded and having a sham exposure. All findings were negative for any effects of either GSM or UMTS exposures on a variety of neurobehavioral task results, when compared to sham exposures. An example is the study by Regel et al. (2006) (cited in Kwon and Hamalainen[5]). They used a controlled randomized double-blinded crossover design to evaluate cognitive performance after exposure to a UMTS base station-like signal at two different strengths and a sham condition. While they did observe some slight but significant differences in speed of the choice reaction time and in reduced accuracy of a separate task (out of 44 tests) at the higher level of exposure, this was no longer significant upon adjustment for multiple comparisons. They concluded that the marginal effects found may be due to chance. Prior studies had problems with poorly defined exposure, inconsistencies in cognitive outcomes and differences in design (such as not taking into account circadian rhythm effects), blinding, study population and sample size.

Examples of studies on neurobehavioral testing: The study by Cinel and colleagues (2008)[18] evaluated effects of mobile phones on short-term memory and attention at two cognitive loads, using a randomized double blinded design.

Methods: A large number of male (n=160) and female (n=168) subjects took part (most being university students) in two experiments. The mobile phone was positioned on the left side of the head for half the subjects and the right side for the others.

For experiment 1, subjects were tested in a manner performing a vigilance task (deciding whether one of three designated letters was shown earlier as a single or string of letters) and n-back task (a short-term memory task choosing a current stimulus which was shown earlier in the sequence; letters and faces were used). In experiment 2, 168 volunteers performed a Stroop attention task (used to study suppression of automatic responses by naming the number of items per string), a Sternberg task (short-term memory, in which four or six black and white pictures were followed by a simple arithmetic calculation, and then a previous picture was shown) and a visual search attention task (random display of 5, 15, or 30 coloured letters, indicating if a target letter was present). The exposure was either to a GSM modulated signal from a mobile phone, to unmodulated signals also having 888 MHz, or to sham. The average SAR (calculated, not measured) was 1.4 W/kg for both phones, but for the GSM mode the peak was 11.2 W/kg.

Results: For experiment 1, the only significant results were related to cognitive load, e.g., the reaction times in the 2-back tasks were faster than the 3-back task. There were no effects of RF exposure on performance for any task (reaction times and accuracy). The authors concluded that there were no significant effects from exposure to RF detected in any of the six tasks used in either the low or high cognitive load conditions. They discounted the results for one task, the Stroop task under a low cognitive condition, where there were faster reaction times in the control condition (i.e., slower times when exposed, although no indication of phone type was given). Accuracy of performance showed an opposite pattern of improvement when exposed to RF. The authors speculate that other aspects of cognitive function, apart from short-term memory and attention, may respond to RF and that longer-term exposure may have an effect on cognitive function.

The aim of the study by Unterlechner and colleagues (2008)[19] was to evaluate the cognitive effects of RF from UMTS signals (as opposed to GSM mobile phones, which were studied previously).

Methods: Young adults (20 men and 20 women; mean age 26 years) had to have no evidence during selection and at each test day of physical or mental illness; physical or psychological overwork; sleep disorders or chronic sleep deprivation; excessive use of caffeine, nicotine or alcohol; or medications. The subjects underwent four different computer tests measuring reaction time and attention under three exposure conditions (high, low, and sham) while in a shielded experimental room.

- The Vienna reaction test registers selective attention through a specific combination of presenting two coloured lights and a tone, given individually or simultaneously.
- The vigilance test measures sustained attention by subjects tracking a leap movement of a shiny point moving clockwise on a circle.
- The Vienna determination test registers divided attention, with the subject reacting to displays of coloured lights and tones.

- The flicker and fusion frequency test registers the optic fusion threshold by determining the frequency when a flickering light becomes constant, and vice-versa.

The order of tests was "pseudo-random" and testing was double-blinded. Exposure was from a generic 3G UMTS signal representing a wideband code division multiple access signal, given at two exposure levels. For the high exposure condition, maximum 10 g-averaged SAR in the brain cortex of the temporal lobe was 0.37 W/kg. Low exposure was 1/10th as much. Subjects sat in a shielded exposure cabin with RF absorbing material on the inner surfaces.

Results: The exposure levels (high, low, and sham) had no effect on any of the different components of attention, as determined by the reaction time, motor activity time and the number of correct and false responses, nor on mean flicker frequency or fusion frequency, nor was there an effect of gender. The authors concluded that a UMTS mobile phone-like exposure does not have an acute effect on attention or reaction time, but the results did not pertain to other cognitive parameters or to long-term effects.

Commentary on the studies by Cinel et al. (2008)[18] and Unterlechner et al. (2008)[19]: The studies used neurobehavioral testing paradigms, which included constructs of attention and vigilance. Cinel et al. added a short-term memory (n-back) task while Unterlechner et al. also evaluated CNS function through testing of the optic fusion threshold. Both studies gave a good description of the tests and their rationale. Positive aspects of the Cinel et al. study were the large sample size and the two levels of "cognitive load" difficulty of the neurobehavioral tasks. However, the conclusion was generalized to there being no significant effects from exposure, despite the data showing that there was a faster reaction time on average in the control condition for the Stroop test; that is, performance was worse during the mobile phone exposure. As well, the rationale given for discounting the Stroop test findings (that it did not correspond to the reaction time results), is not necessarily appropriate, since they may indicate different cognitive functions. In addition, the stringent exclusion criteria such as psychological overwork and taking of medications would affect generalizability of their findings to a large segment of the population.

In the Unterlechner et al. study, testing was done each time in the same period of the afternoon, a voiding possible circadian rhythm effects, but no power calculations were presented as to the choice of only 20 subjects of each sex, which appears to be statistically underpowered. It would have been of interest to use the same protocol but with the GSM exposure as a comparison. Both studies end the discussion with the same caution that other aspects of cognitive function and long-term exposure effects were not assessed and may not have the same findings with regard to the lack of effect of RF.

11.4 Discussion

Widespread and increasing use of wireless technologies has raised concerns about possible health effects associated with exposure to EMF. Canadian and international standards for exposure limits are based on evidence of thermal effects on the human body. The potential for subtle cognitive effects of RF at levels below exposure limits based on thermal mechanisms is controversial. As stated by a scientific panel on EMF health risks[20]: “Life on earth did not evolve with biological protections or adaptive biological responses to these EMF exposures.”

Are there neurophysiological and behavioural effects that can be attributed to exposure to RF?

The general conclusions of the five reviews of provocation studies involving acute exposure to RF (as shown in Table 1) is that there are either no effects or inconsistent results on neurobehavioral parameters and possible minor but inconsistent effects on brain physiology. There is little evidence of acute effects of exposure to RF from mobile phones on cognitive performance or auditory function. Confirmatory research using large representative samples is needed to establish possible effects of exposure to RF on human brain physiology and on cognitive function and performance.

Validity of the laboratory measurements is an important consideration. Have researchers measured appropriate surrogates of cognitive activity? Is an “abnormal” response associated with symptoms or illness? Neurobehavioral tests developed to discriminate differences between “normal” and “neurologically impaired” subjects may not be sensitive in distinguishing more subtle differences in response. On the other hand, effects judged to be harmless when experienced transiently following isolated acute exposures in the laboratory setting may have implications in real-life circumstances, particularly after long-term cumulative exposure to RF.[3]

A further consideration is whether an underlying biological mechanism can be identified to explain effects on brain activity and cognitive performance attributable to exposure to RF. Proposed hypotheses for non-ionizing effects on the brain from RF exposure include interference with brain electric oscillatory activity by pulsed GSM signals and activation of extracellular-signal related kinase (involved in cell signalling).[7] Currently, a mechanism by which RF from mobile phones and other communication devices may interact with neurologic tissue and function is unclear.

A wide variety of neurobehavioral tests have been applied as indicators of such cognitive constructs as short-term memory and attention; yet they lack reliability to sensitively measure the effects of RF exposure. In addition to timing, order and duration of tasks, performance is affected by circadian rhythms and handedness of subjects. Additionally, learning effects may override any treatment effects.[3] More objective measures, such as the EEG, are susceptible to artifacts which can occur with eye or body movements. Not only has the alpha rhythm shown poor scoring

agreement, but up to 20% of the population has little or no measureable alpha rhythm activity under normal circumstances.[7]

Standardization of exposure conditions and detailed reporting would facilitate replicating results in different laboratories. Variation in exposure is known to occur with differences in mobile phone models and technology. For instance, studies on brain activity and behaviour generally show no significant effects of UMTS signals as opposed to the older GSM models with pulsed modulation. Realistically, individuals are exposed to multiple concurrent electromagnetic field exposures over long periods of time. For example, batteries in mobile phones are a source of EMF. Yet for practical purposes, assessing changes in brain function after short-term exposure to one source of RF is the norm.

A disadvantage of laboratory studies on human volunteers is the low power to detect a significant effect.[2] In addition to small sample size, failure to correct for multiple comparisons would result in an increased likelihood of false positive results. This is more likely to occur when there are modest effect sizes and few significant findings among many comparisons. Randomization of subjects and double-blinding help to mitigate possible effects of confounding and bias on the effect estimates obtained. Many of the early studies using single blinding (only the subject was unaware of their exposure status) could not be replicated with a double-blind design.[3,5] Newer studies generally incorporate improvements in study design such as reduced interference from environmental exposure to EMF, adequate study power, and appropriate statistical analysis.

The use of mobile phones, smart phones, tablets and other RF devices is a common form of communication and entertainment for youth, and increasingly so for children. Because the brain is particularly vulnerable to environmental insults during fetal development, childhood and adolescence, there is a need for further studies to ascertain whether there are effects during their developmental stages. For instance, a recent questionnaire-based study on mobile phone use during pregnancy (n=530)[21] concluded that there was no adverse effect on mental or psychomotor development of maternal mobile phone use during pregnancy on the early neurodevelopment of offspring. The anomaly was one statistically significant association of a lower psychomotor score for children whose mothers made at least five mobile phone calls per day in comparison to non-users. Further investigation is warranted to determine potential cognitive effects in children as well as adolescents. According to the AGNIR[22] the few existing relevant studies do not support the hypothesis that children are more susceptible to the effects of RF; however, the evidence is insufficient, particularly due to the small sample sizes in studies so far.

11.4.1 Gaps in the literature

A number of study issues still remain to be addressed to confidently answer the question “Is there convincing evidence of non-cancerous effects on the brain from exposure to mobile phones”:

- determining biological plausible mechanisms of effects on the brain from low exposures to RF in order to characterize what properties of RF may affect neurocognition
- ascertaining whether subtle effects in cognitive function or brain activity manifest as behavioural changes, symptoms, and disability
- improving exposure assessment by considering effects from realistic levels of different mobile phone technologies and evaluating longer-term exposures
- simulating more realistic SARs which take into account the more sensitive nature of brain function (as opposed to absorption in any tissue)
- generalizing isolated laboratory exposures to real life situations of multiple exposures to ambient sources of RF
- including studies of RF effects during growth and development stages, including pregnancy and childhood, and on other vulnerable populations.

11.5 Conclusion

On the basis of current tests of memory and attention, the cumulative evidence to date does not support exposure to RF as having adverse effects on cognitive performance. Where an effect on brain physiology was observed (usually of unknown significance for behaviour or health), there was no corresponding effect on associated neurobehavioral tests.

Detailed measurement of exposure as well as dose, through improvements in the phantom models, will allow for generalizability of findings. In the majority of the study examples given, the SAR was measured to demonstrate that the power of the RF exposures applied was similar to “real world” situations, being less than allowable limits. The technology of wireless communication systems is changing rapidly. The pulsed modulation of the second generation GSM systems appear to have greater effects on neurophysiologic changes than does the third generation UMTS and other developing continuous wave RF applications.

The more consistent findings of EEG changes (particularly alpha frequency spectral power) and the positive results of some of the newer neurophysiologic techniques such as measurement of increased brain glucose metabolism, suggest subtle effects on brain physiology that may be better characterized with new types of measurements and carefully designed replicable larger-scale studies.

Given the broad exposure of the population on a voluntary and involuntary basis to many sources of RF, confirmation of associated effects on neurophysiology and cognitive performance would have important implications for public health. Studies of the pathophysiology of RF need to evolve with improved methodology for determining both exposure (and dose) and effect.

11.6 References

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Section 12

Symptoms Attributed to Radiofrequency Electromagnetic Fields

Table of Contents

Summary

- Electromagnetic hypersensitivity or "EHS" refers to a variety of non-specific symptoms attributed to exposure to electromagnetic fields (EMF), including RF and extremely low frequency (ELF) electrical sources. Prevalence is estimated to vary from 1% to 10% of the population.

- Population health observational studies linking non-specific symptoms with exposure to radiofrequency (RF) waves from mobile phones and mobile phone base stations have shown mixed and inconsistent findings, with a major limitation being poor exposure assessment and biases in the design of the cross-sectional studies.

- In general, subjects who are self-declared with "EHS" in comparison to controls have not been found to reliably detect RF either in experimental conditions (provocation studies) or in their natural environments.

- The results from provocation studies with adequate blinding in place indicate that RF fails to trigger symptoms in self-declared EHS individuals in a reliable, reproducible and consistent way. Sham RF (no exposure) can cause symptoms in EHS persons, and sham shielding may ameliorate symptoms. This supports a possible contribution of a nocebo effect (of symptoms occurring with the expectation rather than actual exposure to RF) to the etiology of EHS.

- Individuals considered to have EHS tend to score significantly higher on personality measures of somatization (conversion of mental states into bodily symptoms) and have a higher likelihood of psychiatric co-morbidity, in particular, somatoform and anxiety disorders. To what extent that these co-morbidities are due the consequences of exposure, rather than to antecedents, needs further investigation.

- The provocation studies are limited to examining short-term exposure to RF and acute symptoms. The effects of cumulative, chronic exposure to RF on human health symptoms have not been well studied.

- Research as well as clinical treatment is hampered by the lack of an accepted and validated case definition for EHS.

12.1 Introduction

Exposure to electromagnetic fields (EMF) has increased over the last century as a result of electricity use and the evolution of wireless technologies such as radio and TV transmitters, satellite signals, mobile phones and mobile phone base stations. EMF exposure is now ubiquitous, and with ongoing technological innovations in wireless technology, this exposure is expected to increase. Considerable public debate and concern have arisen over the potential of adverse health effects of radiofrequency fields (RF) emitted from such diverse sources as mobile phones, wireless internet, particularly in schools (WiFi), "Bluetooth" devices, and smart meters on residences.[1]

A number of people suffering from nonspecific symptoms of unclear origin (symptoms that do not indicate a specific disease process or involve an isolated body system) attribute their health problems to external chemical or physical sources in their environment. A common term for the attribution of symptoms to EMF is "electromagnetic hypersensitivity syndrome" (EHS). People experiencing non-specific symptoms often attribute their health effects to being hypersensitive to the suspected factor at levels well below existing exposure limits.[2] In the case of EMF, attribution is not usually restricted to exposure to specific frequencies but involves a large range of frequencies from extremely low frequencies (ELF) typical of power lines and electrical appliances, to the high frequencies of radiofrequency fields (RF), ranging from 10 MHz to 300 GHz.[2] Wherever possible, this document has focused on literature pertaining to RF, but some pertinent studies including ELF are referenced.

The purpose of this section is to present an evaluation of the scientific literature concerning the association of health symptoms with exposure to RF/EMF.

12.2 Methods

Due to the large volume of literature available on RF and health effects, the literature search focused on reviews of the primary literature. Reviews were identified through a search in PubMed of reviews on EMF and EHS published from 2006 through early 2012, using the MeSH terms "electromagnetic fields" and "adverse effects." We selected reviews written in English and preference was given to systematic reviews and meta-analyses. Four published reviews satisfied our inclusion criteria.[3-6] The studies reviewed by Roosli et al. (2010)[7] overlapped with those of their 2008 and 2011 publications, and therefore this review was not included. Studies on the relationship of EMF with non-specific health symptoms comparing subjects with and without EHS were described as cross-sectional studies on non-specific symptoms in the general population. Case studies were not included because attribution of cause and effect are not possible.

Where available, the following information was extracted from each review: time frame of the review, inclusion/exclusion criteria, aim of the review, methods of exposure/outcome assessment, study design (interventional vs. observational), outcome assessment, effect size and significance.

12.3 Is Electromagnetic Hypersensitivity a Clinical Syndrome?

12.3.1 Terminology and symptoms

The term "Electromagnetic Hypersensitivity Syndrome" (EHS) is widely used in the public media and scientific literature although there are different meanings and alternative definitions. Different terms have been proposed to characterize the impairment for people who attribute their symptoms to EMF, such as "self-reported electric and magnetic field sensitivity."[8] The World Health Organization (WHO) concluded that EHS resembles multiple chemical sensitivities (MCS), another symptom-based condition associated with low-level exposures to chemicals. "Idiopathic Environmental Intolerance" (IEI) was introduced as a neutral term for sensitivity to environmental factors without necessarily implying chemical causation, and now it has replaced the term MCS. The term "IEI-EMF" was proposed to capture symptoms which individuals ascribe to EMF without forming a characteristic symptom cluster;[1] however, use of the term "EHS" persists.

EHS can be loosely defined as a collection of non-specific symptoms of varying degrees of severity that is attributed to environmental electromagnetic fields. Reported symptoms thought by some to be EMF-associated are broad, encompassing neurological, psychiatric, vegetative and dermatological symptoms (Table 1).[2] Symptoms vary between individuals, and so it is difficult to create a uniform case definition.[9,10] Studying individuals who self-identify as persons with EHS is the typical approach used. An early attempt involving 18 European countries failed to identify a specific symptom cluster characterizing a syndrome based on an inquiry.[11]

There is currently no established or accepted clinical diagnosis of EHS supported by the majority of the medical community. The World Health Organization (WHO) states:

> *EHS is characterized by a variety of nonspecific symptoms that differ from individual to individual. The symptoms are certainly real and can vary widely in their severity. Whatever its cause, EHS can be a disabling problem for the affected individual. EHS has no clear diagnostic criteria and there is no scientific basis to link EHS symptoms to EMF exposure. Further, EHS is not a medical diagnosis, nor is it clear that it represents a single medical problem.*[12]

EHS is classified as a functional impairment in Sweden, and Spain has recognized EHS as a permanent disability.[13] According to the Canadian Human Rights Commission, national, provincial and municipal governments all have recognized conditions related to environmental sensitivities, although not necessarily specific to EHS.[14]

Table 1. Reported symptoms ascribed by some individuals to be associated with exposures to EMF

In alphabetical order, obtained from Leitgeb (2009)[2]

Abdominal pain	Headache	Numb limbs
Anxiety	Head pressure	Phosphenes
Appetite loss	Heart beat irregularity	Rash
Arousal decreased	Heart palpitation	Restlessness
Blood pressure increase	Hormonal disorder	Skin burning
Breathlessness	Hypersensitivity to medication	Skin redness
Chest pain	Hypersensitivity to noise	Skin tingling
Concentration difficulties	Intestinal trouble	Sleep disturbance
Crankiness	Irregular bowel movement	Stress
Daytime sleepiness	Irritation	Sweating
Digestive problems	Itching skin	Swollen eyes
Dizziness	Limb pain	Swollen joints
Dry skin	Metabolic disorder	Tachycardia
Exhaustion	Mood changes	Tenseness
Faintness	Mood depression	Tiredness
Fatigue	Muscle cramps	Toothache
Fear	Muscle pain	Trembling
Feebleness	Nausea	Unfeelingness
Feeling hot	Neck pain	Vision blurring
Forgetfulness	Neuralgia	Vomiting
Hair loss	Neurasthenia	Weariness

12.3.2 Differential diagnosis and prevalence

Since EHS is not a recognized clinical diagnosis, the discussion of a differential diagnosis is problematic. It has been suggested that IEI and EHS fall under the broader category of “symptom-based conditions,” or “functional somatic syndromes” which includes other disorders such as sick building syndrome, chronic fatigue syndrome, and Gulf War syndrome. These are not considered to be diseases but descriptions of multisystem symptoms with an associated low threshold of pain or discomfort without corroborating medical signs or pathophysiology.[15] According to Hyams (1998):

> *Although various clinical observations and precipitating events are used for diagnosis, postulated etiologic factors have not been consistently associated with symptom-based conditions. In addition, potential risk factors have not been demonstrated to produce the kinds of organic pathology hypothesized to underlie these conditions…Without verified risk factors, symptom-based conditions are generally thought to have similar multifactorial etiologies and not a single cause. In addition, causal criteria can lead to errors in diagnosis because of reporting bias when a potential cause has been previously emphasized."*[16]

Attempts to define the demographics and/or prevalence of EHS in the few population-based studies that do exist are inherently hampered by subjectivity and the lack of a case definition. The wording of questions asking about EHS strongly influences the assessed prevalence numbers.[2] Patient self-identification is typically used in lieu of a diagnosis.

Considering these limitations, the proportion of the population self-reporting clusters of symptoms such as those listed for "EHS" has been estimated to fall anywhere between 1 and 10% depending upon the location, the age group and definition of EHS used.[13] A population-based cross-sectional questionnaire survey in Sweden of 10,670 adults with a high (75%) response rate reported 1.5% of respondents as being hypersensitive or allergic to electricity.[9] A telephone interview-based study in California of 2,072 adults found 3.2% stating that they were allergic or very sensitive to being near electric appliances, computers or power lines.[17] A similar Swiss study found that 5% of 2,048 people had self-reported EHS.[18] A German population-based cross-sectional study reported that 10.1% of the study sample attributed their adverse health experience (based on a higher summary score from the "Frick" list of 38 health complaints) to mobile phone stations and were possibly exposed, with their residence being 500 m or less away; yet a similar percentage (10.6%) with complaints attributed to mobile phone stations were unexposed, living greater than 500 m away.[19]

In a Swiss study, 71% of individuals with self-reported EHS had symptoms for less than three years, and only 7% experienced symptoms for longer than 10 years; 53% of these individuals reported "very severe" or "severe" physical impairment from their symptoms.[10] In the Californian cross-sectional study (reported above), over one-half of the 3.2% of respondents who indicated that they were allergic or sensitive to common EMF sources reported sensitivities to both EMF and chemicals.[8] In the Swedish study, individuals with self-declared EHS were more likely to report a variety of environmental allergies, including pollen, animal fur, dust mites, and mould, and 31% reported intolerance of dental amalgam.[9] In view of the possible overlap between diverse environmental sensitivities, it is questionable whether EHS constitutes a unique condition or should be considered as part of a broader syndrome.

With respect to the demographics of EHS, these studies suffer from selection bias due to their reliance on self-identification. In general, women and persons with high tendency to somatization (conversion of mental states into bodily symptoms) tend to report more frequent and more severe EMF-associated symptoms.[20]

An association between psychiatric illness and EHS has been observed, but not well-understood. Hypotheses suggest that EHS is either a purely psychiatric somatisation disorder or that psychiatric conditions act as predisposing factors for developing EHS. In terms of personality traits, persons who report symptoms in response to EMF have higher trait anxiety, somatization, and somatosensory amplification scores.[21] Alternatively, there may be neurological and psychological consequences associated with EHS. Signs of mental distress have repeatedly been observed in persons with EMF-related symptoms, e.g., elevated levels of perceived stress, stress susceptibility, anxiety, and depression.[22]

12.4 Electrosensibility and EHS

Sensibility addresses the ability to perceive exposures without necessarily developing health symptoms. *Sensitivity* addresses the development of health symptoms associated with exposures, while for *hypersensitivity,* exposures are at much lower levels than required for the general population.[2]

12.4.1 Electrosensibility in the general population

Leitgeb and Schröttner (2003)[23] tested the ability of a cross-section of the population to detect EMF. The researchers recruited volunteers from a random selection of 200 households in a regional electric utility clients' list (70% response rate) and from visitors of public trade fairs. Volunteers were exposed to electric currents administered via electrodes on their forearms. The currents were increased until the volunteer pushed a button to indicate their perception of current flow. The analysis was performed on 708 adults, aged 17 to 60, including 349 men and 359 women. Women had significantly lower thresholds than men. The relationship between current strength and perception followed a log normal distribution overlapped by a second normal distribution at the sensitive end of low perception thresholds, attributable to EHS cases, with a mean that is 6.7 times lower than the population mean.[23] However, hypersensitive reactions to environmental EMF, characteristics typical for EHS, were expected to be several orders of magnitude (at least one thousand times) below exposure limits, which was not supported by the relatively small difference between population perception thresholds.[2]

12.4.2 Electrosensibility among subjects self- declared as EHS

Central to the postulated diagnosis of hypersensitivity to RF is that individuals self-declared as having EHS are able to discern subthreshold levels of EMF better than the general population. Schrottner and colleagues (2007)[24] studied the electric current perception threshold in three different groups of self-declared EHS patients recruited by different means: (1) an EHS self-help group; (2) a newspaper advertisement; and (3) subjects with health symptoms actively seeking help for perceived RF-induced sleep problems. The results were compared to normal population values. All groups exhibited results overlapping the normal range, with some individuals exhibiting lower-than-normal thresholds in each group. As a whole, the pooled EHS data showed a lowered threshold compared to the population; however, the self-help group showed no

difference from the general population.[24] These results indicated that electrosensibility is a real phenomenon in a proportion of self-declared EHS subjects. However, it remains unknown if these data could be extrapolated to even lower current densities that would reflect more accurately a "hypersensitive" condition. According to Leitgeb (2009)[2] the results demonstrating electrosensibility do not support the hypothesis of "electrohypersensitivity" since the span of results for EHS subjects did not extend beyond the lowest thresholds of the general population. Another consideration is that it was the response to ELF electric currents, and not to RF, that was evaluated.

12.5 Evidence Regarding Electromagnetic Hypersensitivity

12.5.1 Provocation studies

Provocation studies are experimental human studies where subjects are exposed to an agent that is claimed to provoke a response (e.g., mobile phone RF triggering EHS symptoms) and to a sham agent that should provoke no response. Physiological reactions or symptoms occurring during exposure or shortly after provocation (20 minutes to 24 hours) are the endpoints.[6] The degree to which the exposure and testing environment is controlled varies among the different study designs, which in turn, influences the potential for bias and confounding. At one end of the spectrum are the minority of studies which carefully control exposure to RF by using real and sham shielding against EMF in either laboratory or home settings, or by exposing participants to real and sham EMF fields in shielded rooms. Alternatively, many of the laboratory provocation studies create exposures to real and sham mobile-phone-like signals but do not control the background EMF exposure, although they may report or measure this component of exposure.

Experimental provocation study designs have been used to test the ability of individuals to perceive low level RF compared to sham exposure (either directly or via shielding) in order to determine whether individuals with self-reported EHS can perceive EMF. Roosli and colleagues (2008)[3] performed a meta-analysis to evaluate the ability of "EHS" individuals to detect RF emitted from mobile phones or mobile phone base stations. Seven studies met their inclusion criteria encompassing 182 individuals with self-declared EHS and 332 non-EHS individuals. The pooled relative difference between observed and expected correct choices was not statistically significant from zero (averaging 4.2% 95% CI: –2.1 to 10.5).[3] There was no evidence that persons self-reporting as EHS could detect the presence or absence of RF better than persons not considered EHS, that could not be attributed to chance findings. The meta-regression did not show any significant relationship between the ability to detect EMF and EHS status, type of exposure (mobile phone vs. mobile phone base station) or duration of exposure.

Experimental studies have been consistent in demonstrating that acute exposure to RF does not trigger symptoms in individuals with self-reported EHS if they are adequately blinded. Rubin et al. (2010)[25] updated a previous systematic review on provocation studies comparing individuals with and without EHS under blinded conditions.[5] The original meta-analysis of 31 provocation studies reported no robust evidence to

support the existence of EHS. The 2010 update used the same inclusion criteria: subjects had to be exposed to at least two different levels of EMF, the experiment had to be performed under blind or double-blind conditions, and the outcome had to be either self-reported symptoms or the ability to perceive EMF. The review excluded studies that only tested "healthy" participants (i.e., those who did not report EHS).

A total of 46 provocation studies were identified and 16 of these were reviewed in the update. Of the studies selected for the update, seven tested exposure to a mobile phone type signal, four tested exposure to mobile phone base station type signals, four tested exposure to magnetic fields, and one tested the effectiveness of a protective cage over beds of participants reported to have EHS. Subjects were exposed to RF in the 800–900 MHz range with exposures lasting five seconds to 50 minutes. The near-field exposure of the mobile phones all had peak SARs less than 2 W/Kg. For the base station exposures, the whole body exposure to RF was created to have a maximal strength of 10 V/m. For example, in the cited study of Furubayashi et al. in 2009,[26] the subject was exposed to a 2.14 GHz W-CDMA down-link signal at an intensity of about 10 V/m, which corresponds to an incident power density of 0.265 W/m.[2] The result of the meta-analysis was that there was little evidence to suggest that EHS individuals could detect EMF, or EMF triggered acute symptoms. An alternative explanation was the existence of a "nocebo effect" of symptoms occurring with the expectation rather than actual exposure to RF.

These results are in agreement with most other reviews of this area.[3,27,28] The few studies that did report some effects of exposure on participants with self-reported EHS were considered to have methodological flaws due to either type 1 error associated with multiple testing (performing many tests in one study will increase the chance of at least on being incorrectly found to be statistically significant),[29,30] an effect caused by the order of exposure (the order should be given randomly to avoid learning effects)[31] or un-blinding of the study by the participants (who were able to discern shielding from RF exposure and therefore influence the results).[32]

The systematic review by Roosli and colleagues (2008) evaluated whether typical daily levels of exposure to RF are associated with symptoms in self-reported EHS and non-EHS subjects.[3] They selected peer-reviewed studies published prior to 2007 which had non-specific symptoms of ill health as the primary outcome. The exposure had to be in the RF range (300 kHz–3 GHz) and below the International Commission on Non-Ionizing Radiation (ICNIRP) guidelines. Studies were excluded if both exposure and outcome assessment were by self-report alone. In total, 194 "EHS" and 346 non-EHS individuals were included from eight studies. The majority of studies used double blinding and exposure duration was between 30 and 60 minutes. Most often a GSM 900 MHz mobile phone exposure was used, although some studies applied MPBS signals. None of the individual studies found an association between symptoms, and RF exposure and symptoms also tended to occur during the sham exposure.

A study example is the double-blind provocation study by Eltiti et al. (2007)[31] where 56 self-reported "sensitive" subjects and 120 controls were exposed to mobile phone base station-like signals during three exposure conditions (GSM, UMTS and sham). The combined power flux density for each experimental signal was a realistic level of 10 mW/m^2 to the participant. Although the sensitive group reported more symptoms overall, there were no differences between active and sham exposures in the number of symptoms and symptom score for either group. However, during open provocation, when subjects were aware of being exposed or not, the sensitive group did report more symptoms when exposed to either signal compared with sham. The sensitive group had higher skin conductance overall. Judging whether the exposure was "on" or "off" was correctly done by only a few sensitive and control subjects and overall, the judgments by each group did not differ from chance.

Unlike laboratory provocation studies, field studies involve turning EMF sources, such as a mobile phone base station, on/off while participants are in their homes or offices. An example of such a field experiment is the planned shut-down of a short-wave radio transmitter in a Swiss study which determined the effects of RF exposure on salivary melatonin levels and sleep quality of residents living in the vicinity of the transmitter.[33]

The investigators recruited 54 volunteers to take part in two four-day periods of assessment, each of which took place one week before the shut-down of the transmitter (baseline) and one week after. The researchers grouped subjects into low and high exposure on the basis of estimated average 24-hour exposure for each participant's home as determined by the relative position of the residence to the centre of the antenna and exposure measurements at baseline, which took place in 1992, 1993, and 1996. The transmitter operated at frequencies of 6.1 to 21.8 MHz, and after shut down there were no other exposures in this frequency range. Volunteers collected two samples of their own saliva at five different times during the day and filled out a sleep diary every morning, reporting morning tiredness, sleep quality, duration of sleep and the time that they fell asleep.

After controlling for age and gender, and taking into account baseline measurements in a regression analysis, subjects rated their morning freshness as 1.74 units better for each mA/m reduction in magnetic field exposure, which was statistically significant (with a 95% CI of 0.11 to 3.36 which does not include zero, or no difference). Melatonin excretion tended to be increased (although not statistically significant) by 15% (95% CI: –3 to 36%). Blinding of the subjects to the exposure source was not possible in this study. Furthermore, there is the potential for biased results in the sleep diary since this study was developed from an investigation that was initiated by residents' symptomatic complaints.

Roosli and colleagues (2011) updated their 2008 review to evaluate studies published between 2007 and 2011. Nine experimental studies investigated exposures close to body sources (using GSM 900 mobile phones, tetra handsets and UMTS phones) and

six experimental studies determined the effects of far-field sources either in the laboratory or under everyday environments. Almost all of the nine experimental studies of RF exposures from phones and handsets showed no increase in any symptom during exposure and most of the six experimental far-field studies were also negative. It was concluded that the 15 randomized trials showed little evidence that short-term RF exposure causes non-specific symptoms.

12.5.2 Limitations of provocation studies

Provocation studies allow greater control over confounding variables and exposures and therefore the possibility of biased results is minimized. Although this design provides the temporal association that is necessary for causal inference, it only allows for assessment of the acute effects of short-term exposure. In a recent review of study criteria used to define IEI-EMF by Baliatsas et al. (2012), a major inclusion criteria for identifying EHS was the experience of symptoms during or soon after the perception or presence of an EMF exposure source (from 20 minutes to 24 hours after).[6] Yet symptoms associated with exposure to RF can be chronic, developing over time with low levels of exposure. Furthermore, individuals may react to a specific EMF frequency from a source that is not being tested in the experimental protocol[13] or to multiple sources of RF simultaneously.

An additional drawback to this experimental study design is the small sample size, which therefore leads to low statistical power, and limited ability to detect relatively rare effects. The laboratory setting itself may provoke anxiety in participants and may introduce noise into the study, masking any subtle induced symptoms. In addition, it is possible that by controlling for all background exposure through use of shielded exposure rooms, some unknown synergistic elements of EMF may also be removed. An alternative is conducting experiments in “real-life” settings such as residences or workplaces. However, the level of control over the extent of exposure and confounding variables is even more difficult to achieve than in laboratory experiments.

12.5.3 Observational studies

There is a large body of observational research that explores the relationship between EMF and non-specific health effects. The prospective cohort design (subjects who are initially free of disease are followed forward in time) is considered to be stronger than cross-sectional designs in determining causal relationships. There are currently no reports of prospective cohort studies evaluating the relationship of exposure to RF to the development of non-specific symptoms characteristic of EHS.

The cross-sectional design is the most frequently used for evaluating symptomatic responses to exposure to RF. Information about a wide range of health outcomes is collected by questionnaire, with standardized instruments available to assess symptoms. Most studies were population-based rather than focusing on “EHS” subjects.

Although a limited number of studies have addressed the effects of near-exposure RF (close-to-body), e.g., mobile or cordless phone use, the majority of researchers have attempted to evaluate the effects of far-field RF exposure. The exposure type and methods of exposure ascertainment in these studies vary greatly. Exposure sources include a single mobile phone base station (MPBS), all MPBS in the vicinity of a residence, and the sum of EMF from MPBS stations and WiFi. Exposure assessment is usually based on distance from the residence to the exposure source (typically an MPBS), spot measurements in bedrooms and offices, or personal dosimetry of total RF over the course of a waking day or a 24-hour period.

All of these methods for exposure assessment have limitations which affect accuracy of the measurement of RF (see Section 5). While, the exposure levels generally decrease substantially with increasing distance (inverse square law) in the far field of base stations, the exposure levels are affected by reflections from buildings and other obstacles. A better predictor of exposure than distance is line-of-sight to the base station. The representativeness of personal dosimetry of RF is complicated by the low levels found and variability due to changing multiple sources of exposure and the dominant contributions of mobile phone technology.

Roosli (2008)[3] reviewed the findings of observational population-based studies and found that results differed from those of the provocation studies. A statistically significant positive association was reported for the association of exposure with symptoms for each of four cross-sectional observational studies, although the type of exposures, exposure assessment and health outcomes considered varied greatly. For instance, a Swiss cross-sectional survey queried 400 adults living at various distances from a short-wave broadcast transmitter about their sleep and other somatic symptoms. Exposure assessment was based on 2,621 measurements of magnetic field strength in 56 locations. The study found a significant relationship for difficulty in falling asleep, maintaining sleep, tiredness, nervousness and restlessness in the more exposed.[34] However, the authors do report that this series of studies was instigated by similar symptomatic complaints by residents living near the broadcast transmitter and the subjects could not be blinded to their exposure. An Austrian study surveyed 365 randomly selected individuals living near a MPBS about subjective symptoms, sleep, and cognitive performance. Exposure measurements were based on spot measurements of high frequency EMF taken in the bedrooms of the participants after completion of the questionnaire. The symptoms of headache, cold hands or feet and concentration difficulties were significantly associated with exposure levels, even after their response of fear of negative effects was taken into account.[12] Exposure levels were generally low (95% were below 1 mW/m^2) for frequencies ranging from 80 MHz to 2 GHz and the contribution was mostly from mobile communications. Concerns about negative health effects associated with living near a MPBS were highly related to overall sleep quality.

The 2011 narrative review by Roosli and colleagues,[4] an update of the 2008 review,[3] explored the effects of RF exposure encountered in everyday life on self-reported non-

specific symptoms and well-being, as was also covered extensively by Roosli et al. (2010).[7] They included eight studies published from 2007 to 2010 with RF-exposure frequencies ranging from a few MHz up to 10 GHz and excluded studies based on self-reported exposure.

Only three of the eight studies reported statistically significant associations. The authors noted a lack of association of exposure to RF and symptoms found in the majority of recent observational studies, contradicting the findings of their earlier (2008) review.[3] As well, cross-sectional epidemiological studies with crude exposure assessments based on distance from an RF source often showed health effects, whereas studies based on more sophisticated exposure measurements rarely indicated any association.[7] Whether there are unknown confounders related to socioeconomic or other conditions which are related to residence near a base station that may explain the increase in symptoms is not known. Alternatively, there may be characteristics of RF relevant to health not captured by measurement of power density.

An example of a large cross-sectional study is the investigation the relationship between MPBSs and self-reported health and well-being in a representative population of German residents.[19] In the first phase of this study, 26,039 subjects aged 14 to 69 completed a questionnaire about a variety of health symptoms. Exposure to RF was based on the distance between a participant's address and the nearest mobile phone base station, where a distance of ≤500 m was considered possible exposure and a distance > 500 m was considered non-exposure. In this study, 18.7% were concerned about health effects from MPBSs and 10% attributed their health effects to MPBSs. Multivariate linear regression analysis was conducted for a 38 item symptom list adjusted for gender, age, income, education, region of residence, urban vs. rural, concern about MPBSs, attribution of health effects to MPBSs and distance to the nearest MPBS. Participants who had possible exposure to RF by living closer to an MPBS scored slightly higher on the Frick Summary Symptom Score (indicating greater severity) than less exposed residents.

In the second phase of the study, a subset of individuals who participated in Phase I of the study also had dosimetry performed in their homes.[35] Five standardized health questionnaires were used to measure sleep disturbances, headaches, health complaints, mental health and physical health. Exposure information was obtained through combining dosimetric measurements of five minutes each in four different positions on the beds of participants. In each location, 75 measurements were taken for 12 different frequency ranges, encompassing frequencies from 88 MHz to 2.5 GHz. Uplink frequencies used for communication between mobile phones and mobile phone base stations were excluded from the calculation of the "mean total field value," as the study focus was background RF. A person living in a residence with a mean total field >0.1 V/m (0.029 mW/m^2) was considered exposed.

Of 1,326 participants with valid RF measurements, 27.1% were concerned about MPBS and 8.8% attributed their health problems to EMF. Exposures were generally found to

be low; 65.8% of the households had a total mean field value below 0.05 V/m (limit of detection) and the highest value was 1.14 V/m. No differences in the medians of the five health scores were observed for the comparison of exposed versus non-exposed, whether based on RF from mobile telecommunication frequencies or total RF including exposures from TV and radio broadcast towers, cordless phone base stations and WiFi. The authors concluded that measured RF (analyzed only as a binary variable) emitted from mobile phone base stations was not associated with adverse health effects. However, the researchers noted that subjects attributing adverse health effects to MPBSs had more sleep disturbances and health complaints.

Baliatsas and colleagues (2012)[6] conducted a formal systematic review of observational studies published between 2000 and 2011 regarding symptoms attributed to actual and perceived exposure to EMF among the general population. Of the 22 studies included as having adequate reporting quality (of 41 eligible articles), 13 studies provided data on actual exposure to EMF based on field strength spot measurements, use of personal dosimeters during waking hours, exposure predictor modeling or geo-coded distance to base stations, with eight studies using standardized instruments to assess non-specific physical symptoms (NSPS). The results of nine of the 13 studies showed an association with at least one symptom. The number of studies where there was a significant effect of actual exposure on NSPS (versus the negative studies) was as follows: fatigue (n=1 vs. 4); concentration difficulties (n=1 vs. 3); headache (n=4 vs. 3); sleep problems (n=4 vs. 5); and dizziness (n=3 vs. 3).

Methodological quality was determined to be an important component for the strength of the associations, since studies with questionable exposure assessment and/or sample selection reported more significant associations. More recent studies using advanced exposure characterization methods did not suggest a significant effect. Although there were only two to four studies contributing to the analysis of each symptom group, there were between 919 and 1897 study participants included in each analysis. Meta-analyses were conducted to quantify the association, after excluding five studies due to high risk of bias and lack of comparability. No significant effect of higher exposure levels was determined for any of the symptoms analyzed according to severity (acute) and frequency (chronic). The investigators concluded that there were no indications for an association between higher levels of actual EMF exposure and frequency and severity of NSPS in the general population. It was recognized that the meta-analysis was limited by the small number of available high quality comparable studies.

Twelve studies reported on the association between perceived exposure and NSPS, based on daily use (duration and/or number of calls) of mobile phones. Seven studies assessed symptoms with standardized instruments. Comparison of the number of studies showing a significant effect of perceived exposure on NSPS (versus negative studies) were: concentration problems (n=4 vs. 2); headache (n=5 vs. 3); fatigue (n=4 vs. 3); burning sensation (n=2 vs. 2); sleep problems (n=1 vs. 4); and dizziness (n=2 vs. 5). Due to the considerable heterogeneity between studies, meta-analysis could not be

performed. It was concluded that, unlike the studies measuring EMF exposure, there may be an association of symptoms with perceived exposure, although more evidence is needed due to the lack of comparable methods and instruments to assess perceived exposure and outcomes between studies.

12.5.4 Limitations of observational studies

There have been a large number of cross-sectional studies conducted on RF and non-specific health effects. Cross-sectional studies are regarded as a relatively weak epidemiological design as they are subject to bias related to design and confounder effects, as well as misclassification of exposure and effects. Overall, cross-sectional studies have reported more positive associations between EMF exposure and EHS symptoms than other types of studies, particularly for perceived exposure, but the findings are frequently mixed. For example, a statistically significant association was found between "skin tingling" and mobile phone use in a Scandinavian study,[36] while only a trend was identified in a Singaporean study,[37] and no association at all was found in a French study.[37,38] Cross-sectional studies have the potential to assess the effects of long-term exposures, but the temporal relationship is difficult to establish, and it is generally not possible to blind participants, leading to considerable risk of information bias.

Exposure classification is challenging for most observational studies, given the many different sources of RF exposure in the environment. These exposures vary significantly with time and are heterogeneous. Hence, non-differential misclassification is a problem for observational studies, which biases study outcomes towards the null. In older cross-sectional studies, the exposure assessment was frequently based on distance from transmitters, but dosimetry subsequently revealed that distance did not correlate well with actual levels of exposure. In addition, exposure to RF is low overall, leading to low variability and lack of an exposure gradient, which makes finding an effect, if there is one, more difficult.

12.6 Nocebo Effect

With adequate study blinding, subjects considered to have EHS generally are not able to perceive levels of RF, or even the presence of RF. In the placebo-controlled studies that used sham exposure or sham shielding, symptoms were elicited by both the active and the sham conditions (reviewed in Rubin et al. (2010)[5]). The observation that sham conditions are able to provoke symptoms supports the role of nocebo effects in the etiology of EHS. Nocebo is an undesirable effect resulting from the suggestion or belief that something is harmful, when it is not. It has been noted that symptom scores in provocation studies are related to the beliefs about the actual presence or intensity of EMF.[39] The role of negative expectations in triggering symptoms is supported by a recent study in which 40 college students were asked to rate their symptoms during "sham," "weak," and "strong" RF exposure. In reality, there was no exposure at all, i.e., all sessions were "sham." Suggestions of stronger EMF exposure resulted in higher symptom scores and enhanced EMF-perception.[40]

Roosli et al. (2010, 2011)[4,7] observed that cross-sectional studies which used crude exposure measurements based on distance tended to show health effects, while studies which used more sophisticated measures of exposure, such as dosimetry, rarely found an association. In the 2011 review evidence suggestive of a nocebo effect was discussed.[4] In a double-blind, randomized, cross-over control study using exposure to Universal Mobile Telecommunication System (UMTS) signals, a significant association was observed between symptom score and perceived field intensity in both "EHS" and non-EHS individuals even though perceived fields were not associated with exposure levels.[41] Likewise a strong correlation between symptom score and perceived operating status was observed in the field trial of the UMTS base station ($p<0.0001$).[42] In another laboratory study, both individuals with and without reporting of EHS felt worse and had more severe symptoms during exposure to a TETRA mobile phone base station during open provocation compared to sham, with a greater effect seen in individuals considered to have EHS. The effect disappeared in subsequent double-blind testing where no differences were found between exposure and sham conditions for symptomatic or physiological measures.[43] These results support the observation that a nocebo effect may be apparent for symptoms associated with EHS and should be considered in study designs.

12.7 Discussion

Research in this area is hampered by issues of internal and external validity of the studies, which limit the inferences that can be made. For example, the existence of a nocebo effect, associated with the expectation of reacting negatively to exposure, highlights the importance of using blinding techniques in provocation studies.

There is much heterogeneity of exposure measurement regarding the EMF frequencies used, their pulsing characteristics, on-off behavior and the variable contributions of ELF and RF. In provocation studies, exposures range greatly in terms of type, strength and duration. There is uncertainty about the characteristics of RF exposure which are important for health. The observation that dosimetric measurement of exposure is usually not associated with health effects (unlike crude distance measurements) may be related both to the variability (and subsequent misclassification) of personal exposure measurements as well as the role of perception of exposure on symptoms. Multiple sources of exposure to RF are an important consideration in studies of "real-life" exposures.

Studies utilize a variety of symptom lists for non-specific health symptoms and include a diverse array of outcomes such as cognitive effects, sleep disturbance, headaches, neurological disorders and somatic complaints. This reflects the wide range of health symptoms in individuals who report that they have EHS. There is a lack of an accepted and validated case definition for EHS. Applying broad criteria not only dilutes the power of studies to determine an outcome for self-reported EHS subjects, but there is also a greater potential for misclassification and inability to detect legitimate subjects considered to have EHS.

While EHS may not have an accepted clinical definition, subjects who self-identify as EHS can be severely debilitated by their symptoms. The prominent contribution of the nocebo effect in the generation of the symptoms of EHS should not be ignored, nor should it be used as a means to disregard symptoms. Rather, it should be seen as a disease-causing mechanism in itself, termed the "psychogenic" model of EHS.[15]

Grouping symptom-based illnesses together, including illnesses such as MCS, chronic fatigue syndrome and fibromyalgia could benefit from similar—although individually tailored—approaches to multidisciplinary management. In this regard, there are small studies of EHS patients responding well to sleep hygiene, avoidance/reduction of triggers,[13] cognitive behavioral therapy,[44] and anxiolytics.

The decades of research regarding symptoms in the general population attributed to exposure to EMF have been hampered by a lack of clear definition of what constitutes a diagnosis of "EHS." Cross-sectional and provocation studies generally rely on self-report of EHS, which introduces problems of misclassification and affects the strength of any association found.

Further research is needed to define what types of EMF exposure may be of relevance, what biological mechanisms may be involved and the role of chronic exposure to EMF on symptoms and reporting of EHS. Since most studies have been conducted on adults, the symptomatic effects of exposure to RF on children and other potentially vulnerable groups are not clear.

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Section 13

Radiofrequency Safety Guidelines and Standards

Table of Contents

13.1 Canada – Health Canada's Radiofrequency (RF) Exposure Guidelines: Safety Code 6

The current update of Safety Code 6 titled "Limits of Human Exposure to Radiofrequency Electromagnetic Energy in the Frequency Range from 3 kHz to 300 GHz"[1] was released by Health Canada in 2009. It replaced the 1999 version (99-EHD-237).

Safety Code 6 applies to workers and to the general public.

In this section of the toolkit, the focus will be on the exposure of the general public.

Excerpts (*in italics*) from Safety Code 6 (SC.6) with BCCDC comments:

SC.6 Part 1 – Preface (Page 3 of the Code)

1.1 - "This code has been adopted as the scientific basis for the equipment certification specifications outlined in Industry Canada's regulatory compliance documents that govern the use of wireless devices in Canada, such as cell phones, cell towers (base stations) and broadcast antennae."

Comment: This statement is consistent with the recommendations of the International Commission on Non-Ionizing Radiation Protection (ICNIRP).

1.2 – "The guidelines (exposure limits) do not apply to the deliberate exposure for treatment of patients by, or under the direction of, medical practitioners."

Comment: RF sources of different frequencies and power outputs are used in medicine (radiology, oncology, cardiology, physiotherapy) for diagnostic and therapeutic purposes. In general, there are no exposure limits pertaining to patients, but some precautions are recommended by ICNIRP.

1.3 – "The guidelines are not intended for use as a product performance specification document, as the limits in this safety code are for controlling human exposure and are independent of the source of RF energy."

Comment: Product performance specifications relate to the design and quality of the products. They fall under the responsibility of Industry Canada (IC). IC regulations apply to RF installations and devices, such as radio-communication and broadcasting antenna systems[2] and radio-communication apparatus at all frequency bands.[3]

1.4 – "The safety limits in this code are based on an ongoing review of published scientific studies on the health impacts of radiofrequency electromagnetic energy. This code is periodically revised to reflect new knowledge in the scientific literature and the exposure limits may be modified, if deemed necessary."

Comment: On the whole, Safety Code 6 guidelines are consistent with the recommendations of the International Commission on Non-ionizing Radiation Protection[4,5] and the recommendations of the World Health Organization.[6] Currently, ICNIRP is reviewing its RF guidelines, but no date has been set for the completion of this work. We would expect Health Canada to follow suit if major changes are made to ICNIRP's RF guidelines.

SC.6 Part 2 - Introduction (Pages 7- 8)

2.1- Page 7 – "The exposure limits specified in Safety Code 6 have been established based upon a thorough evaluation of the scientific literature related to the thermal and possible non-thermal effects of RF energy on biological systems.

Health Canada scientists consider all peer-reviewed scientific studies, on an ongoing basis, and employ a weight-of-evidence approach when evaluating the possible health risks of RF energy.

This approach takes into account both the quantity of studies on a particular endpoint (whether adverse or no effect), but more importantly, the quality of those studies.

Poorly conducted studies (e.g., incomplete dosimetry or inadequate control samples) receive relatively little weight, while properly conducted studies (e.g., all controls included, appropriate statistics, complete dosimetry) receive more weight."

2.2- Page 8 – "The purposes of the Code are:

(a) Specify maximum levels of human exposure to RF energy at frequencies between 3 kHz and 300 GHz, to prevent adverse human health effects;

(b) Specify maximum allowable RF contact and induced body currents to prevent the physical perception of internal currents resulting from RF energy in uncontrolled environments, and to prevent RF shock or burns to personnel in controlled environments;

(c) Provide guidance for evaluating RF exposure levels to ensure that personnel in controlled and uncontrolled environments are not exposed at levels greater than the limits specified in this code."

Comment: Safety Code 6 guidelines are based on review of both thermal and non-thermal effects.

Note: controlled environment refers to worker environment and uncontrolled environment to public spaces.

SC.6 Part 3 - Maximum exposure limits (Pages 9–21)

3.1- Page 9

- *"Despite the advent of thousands of additional research studies on RF energy and health, the predominant adverse health effects associated with RF energy exposures in the frequency range from 3 kHz to 300 GHz still relate to the occurrence of tissue heating and excitable tissue stimulation from short-term (acute) exposures."*
- *"At present, there is no scientific basis for the premise of chronic and/or cumulative health risks from RF energy at levels below the limits outlined in Safety Code 6."*
- *"For frequencies from 3 to 100 kHz, the predominant health effect to be avoided is the unintentional stimulation of excitable tissues, since the threshold for electro-stimulation in this frequency range will typically be lower than that for the onset of thermal effects.*

Experimental studies have demonstrated that exogenous electric and magnetic field exposures can induce in situ electric fields and currents within biological tissue that can lead to nerve and muscle depolarization (5, 8–9, 31–32).

Limits for maximum external electric and magnetic field strengths have been established in Safety Code 6 to avoid in situ electric field strengths greater than that of the minimum excitation threshold for excitable tissues."

- *"For frequencies from 100 kHz to 300 GHz, tissue heating is the predominant health effect to be avoided. Other proposed non-thermal effects have not been conclusively documented to occur at levels below the threshold where thermal effects arise. Studies in animals, including non-human primates, have consistently demonstrated a threshold effect for the occurrence of behavioral changes and alterations in core-body temperature of ~1.0°C, at a whole-body average SAR of ~4 W/kg. This forms the scientific basis for the whole-body average SAR limits in Safety Code 6. To ensure that thermal effects are avoided, a safety factor of 10 has been incorporated for exposures in controlled environments, resulting in a whole-body-averaged SAR limit of 0.4 W/kg.*

  <u>A safety margin of 50</u> has been incorporated for exposures in uncontrolled environments to protect the general public, resulting in a whole-body average <u>SAR limit of 0.08 W/kg.</u>"

<u>Comment</u>: RF devices used by the general public operate at frequencies ranging from 300 kHz to 2.45 GHz. Thus, the main interest is on frequencies above 300 kHz. As stated in Safety Code 6, the thermal effects due to absorption of radiofrequency energy by soft tissue are the main basis for regulation. The exposure limits have been set to prevent excessive tissue heating. The rate at which RF energy is absorbed by the body is described in terms of the Specific Absorption Rate (SAR) in units of Watt/Kilogram (W/Kg). For reference, a list of SAR values for Cellular Telephones has been made available by the US Federal Communication Commission.[7]

3.2- Exposure limits for public areas – Safety Code 6 Exposure Limits[1(Table 6, p. 18)]

Table 6. Exposure Limits for Uncontrolled Environments.

1 Frequency (MHz)	2 Electric Field Strength; rms (V/m)	3 Magnetic Field Strength; rms (A/m)	4 Power Density (W/m^2)	5 Averaging Time (min)
0.003 - 1	280	2.19		6
1 - 10	$280/f$	$2.19/f$		6
10 - 30	28	$2.19/f$		6
30 - 300	28	0.073	2*	6
300 - 1 500	$1.585f^{0.5}$	$0.0042f^{0.5}$	$f/150$	6
1 500 - 15 000	61.4	0.163	10	6
15 000 - 150 000	61.4	0.163	10	$616\,000/f^{1.2}$
150 000 - 300 000	$0.158f^{0.5}$	$4.21 \times 10^{-4}f^{0.5}$	$6.67 \times 10^{-5}f$	$616\,000/f^{1.2}$

* Power density limit is applicable at frequencies greater than 100 MHz.

Notes: 1. Frequency, f, is in MHz.
2. A power density of 10 W/m^2 is equivalent to 1 mW/cm^2.
3. A magnetic field strength of 1 A/m corresponds to 1.257 microtesla (μT) or 12.57 milligauss (mG).

- ICNIRP's Exposure Limits[4] *(Table 7, p. 511)*

Table 7. Reference levels for general public exposure to time-varying electric and magnetic fields (unperturbed rms values).[a]

Frequency range	E-field strength ($V m^{-1}$)	H-field strength ($A m^{-1}$)	B-field (μT)	Equivalent plane wave power density S_{eq} ($W m^{-2}$)
up to 1 Hz	—	3.2×10^4	4×10^4	—
1–8 Hz	10,000	$3.2 \times 10^4/f^2$	$4 \times 10^4/f^2$	—
8–25 Hz	10,000	$4,000/f$	$5,000/f$	—
0.025–0.8 kHz	$250/f$	$4/f$	$5/f$	—
0.8–3 kHz	$250/f$	5	6.25	—
3–150 kHz	87	5	6.25	—
0.15–1 MHz	87	$0.73/f$	$0.92/f$	—
1–10 MHz	$87/f^{1/2}$	$0.73/f$	$0.92/f$	—
10–400 MHz	28	0.073	0.092	2
400–2,000 MHz	$1.375f^{1/2}$	$0.0037f^{1/2}$	$0.0046f^{1/2}$	$f/200$
2–300 GHz	61	0.16	0.20	10

Comment: There are differences between Safety Code 6 and ICNIRP power density limits in the frequency range 300 MHz-1500 MHz. Canada and the United States apply a limit of f/150 for frequencies between 300 MHz and 1.5 GHz while ICNIRP recommends a limit of f/200, f being the frequency in MHz.

For example, at a frequency of 900 MHz, the Canadian limit is 900/150 = 6 Watt/m^2 (600 $\mu W/cm^2$) while ICNIRP's limit is 900/200 = 4.5 Watt/ m^2 (450 $\mu W/cm^2$).

However, this has little practical impact on the protection of the public since the time-averaged power densities from existing domestic devices are much lower even at close distances. For example, the power densities from RF devices such as baby monitors, microwave ovens, mobile phones, Wi-Fi, and smart meters are less that 0.01 Watt/m^2 at 1 meter from the source.

13.2 Guidelines of the International Commission on Non-Ionizing Radiation Protection (ICNIRP)

"Guidelines for limiting exposure to time-varying electric, magnetic and electromagnettic fields (up to 300 GHz)"[4]

ICNIRP's limits of exposure to electromagnetic fields (EMF) are based on established health effects and are termed reference levels. Depending on the frequency and the exposure conditions, the physical quantities used to specify the exposure limits are: current density, SAR, and power density.

Excerpts (*in italics*) from ICNIRP guidelines with BCCDC comments:

ICNIRP-Page 510: Guidelines for limiting EMF exposure –

The basic restrictions for time varying electric and magnetic fields are for frequencies up to 10 GHz. The health effects considered in the development of basic exposure restrictions for various frequency ranges are:

- *"Between 1 Hz and 100 KHz, basic restrictions are provided on current density to prevent effects on nervous system functions."*

Comment: In the frequency range 1 Hz–100 kHz, the thermal effects are negligible and the induced currents generated by magnetic fields are the main concern. The limits are intended to prevent peripheral nerve and/or cardiac stimulation.

Example of sources in the frequency range 1 Hz–100 kHz: electrical power lines (50–60 Hz), MRI magnetic fields, electrical appliances, radio navigation, industrial induction heaters, etc.

- *"Between 100 kHz and 10 GHz, basic restrictions on SAR are provided to prevent whole-body heat stress and excessive localized tissue heating; in the 100 kHz–10 MHz range, restrictions are provided on both current density and SAR."*

Comment: At frequencies between 100 kHz and 10 GHz, the thermal effects are predominant. Therefore, the limits apply to the specific absorption rate (SAR).

Example of sources in the frequency range 100 kHz–10 GHz: AM/FM radio, shortwave radio, CB radio, TV, mobile phones and base stations, microwave ovens, radar, etc.

- *"Between 10 GHz and 300 GHz, basic restrictions are provided on power density to prevent excessive heating near the body surface (skin)."*

Comment: Above 10 GHz and up to 300 GHz, the penetration of RF energy into tissue is weak, and most of the incident energy is absorbed at the surface of the skin. As a result, SAR is negligible in this frequency range and power density is the appropriate quantity to measure.

Example of sources in the frequency range 10 GHz–300 GHz: Transmission video devices (remote sensing, security screening, telecommunications by satellite, etc.).

- *"In the low-frequency range up to 100 kHz, the general public reference levels for magnetic fields are set at a factor of 5 below the values set for occupational exposure."*

- *"In the frequency range 100 kHz–10 MHz, the general public reference levels for magnetic fields have been increased compared with the limits given in the 1988 IRPA guideline. In that guideline, the magnetic field strength reference levels were calculated from the electric field strength reference levels by using the far-field formula relating E and H."*

- *"In the high-frequency range 10 MHz–10 GHz, the general public reference levels for electric and magnetic fields are lower by a factor of 2.2 than those set for occupational exposure. The factor of 2.2 corresponds to the square root of 5, which is the safety factor between the basic restrictions for occupational exposure and those for general public exposure."*

Comment: In the far field, the electrical field E is proportional to the square root of the power density: E= $\sqrt{\boldsymbol{S}}$

The occupational power density limit $\mathbf{S(W)_{limit}}$ is equal to five times the public power density limit $\mathbf{5 \text{ x } \boldsymbol{S}(\boldsymbol{P})_{limit}(\boldsymbol{public})}$:

$$\boldsymbol{S}(\boldsymbol{W})_{\boldsymbol{limit}}(\boldsymbol{workers}) = \mathbf{5 \text{ x }} \boldsymbol{S}(\boldsymbol{P})_{\boldsymbol{limit}}(\boldsymbol{public}),$$

Then:

$$\boldsymbol{E}_{\boldsymbol{limit}}(\boldsymbol{workers}) = \sqrt{\mathbf{5}}\, \boldsymbol{E}_{\boldsymbol{limit}}(\boldsymbol{public}) = \mathbf{2.2}\, \boldsymbol{E}_{\boldsymbol{limit}}(\boldsymbol{public})$$

- *"In the high-frequency range 10–300 GHz, the general public reference levels are defined by the power density, as in the basic restrictions, and are lower by a factor of 5 than the occupational exposure restrictions."*

Comment: At high frequencies above 10 GHz, RF waves are much less penetrating and rapidly absorbed by the skin. As a result, the internal thermal effects are insignificant and the assessment of SAR is inappropriate. Therefore, only power density measurements are necessary above 10 GHz.

13.3 Other RF Guidelines

USA

In the United States, the **Federal Communications Commission** (FCC) regulates interstate and international communications by radio, television, wire, satellite and cable in all 50 states, the District of Columbia, and US territories.

On August 1, 1996 the FCC adopted the RF guidelines developed by the National Council on Radiation Protection and Measurements (NCRP): "Maximum Permissible Exposure limits for field strength and power density for the transmitters operating at frequencies of 300 kHz–100 GHz."[8]

The Commission adopted also the RF standards developed by the **Institute of Electrical and Electronics Engineers** IEEE-C95.1–2005 Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz.[9]

Comment: At 900 MHz, the FCC RF power density limits are 33% higher than ICNIRP reference levels. For other frequencies, the FCC limits are similar to ICNIRP's.

United Kingdom (UK)

Advice on limiting exposure to electromagnetic fields between 0 and 300 GHz – NRPB-Volume 12, No. 2, **2004**.[10]

Comment: The UK guidelines are based on ICNIRP recommendations, with the same exposure limits.

Australia: Australian Radiation Protection and Nuclear Agency (ARPANSA)

Regulations: Maximum exposure levels to RF fields – 3 kHz to 300 GHz (adopted on 20 March 2002).[11]

Comment: Australian guidelines are based on ICNIRP recommendations, with the same exposure limits.

Switzerland

In Switzerland,[12,13] an ordinance on the protection against non-ionizing radiation was adopted in 1999. RF exposure limits similar to ICNIRP's reference levels apply in all public areas.

However, lower precautionary limits are added as follows:

- A limit for the electric field E of **10% of ICNIRP reference level** (equivalent to **1% of ICNIRP power density** reference level) applies to mobile base stations.

- Frequency-dependent exposure limits for electrical field strength E of **11% to 3% of ICNIRP reference levels** apply to other RF transmitters and radar.

Russia

In Russia, the protection of the population is governed by the Law 2.2.4/2.1.8.055-96 on "Sanitary norms and regulations."[14] Exposure limits are based on "Hygienic-epidemiological requirements" and equal to 2% of ICNIRP reference levels for RF fields in the frequency range 300 MHz–300 GHz. The basis of the Russian limits is to "prevent biological effects that are not generally seen as health risk in Western countries."[13]

European Union (EU)

The EU issued a Directive on RF in 2004: Directive 2004/40/EC of the European Parliament and of the Council of 29 April 2004 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (electromagnetic fields) - Frequencies Covered: > 1 Hz – 300 GHz[15]

Comment: The European Union Directive is based on ICNIRP recommendations, with the same exposure limits. However, EU countries adopted three different approaches, as shown in Table 1.[13]

Table 1. Different regulatory approaches by EU countries

Group	Countries	Regulations	National RF limits	Basis
G1	Cyprus, Czech republic, Estonia, Finland, France, Hungary, Ireland, Malta, Portugal, Romania, and Spain	Yes, mandatory. Identical to EU Directive 2004/40/EC	Based on ICNIRP reference levels	As ICNIRP, science-based
G2	Austria, Denmark, Latvia, Netherlands, Sweden, UK	No binding regulations	Recommended limits based on ICNIRP reference levels but not mandatory.	As ICNIRP, science-based
G3	Belgium, Bulgaria, Greece, Italy, Lithuania, Luxembourg, Poland, Slovenia	Yes, mandatory. More stringent rules than EU Directive	1% of ICNIRP reference levels	Precautionary principle, public pressure

13.4 Comparison of exposure limits in different countries

Most countries follow the recommendations of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) for limiting exposure to RF fields. However, some differences exist between North America, Eastern Europe and Western Europe.

Table 2 below[13] shows the RF exposure limits for the general public in different countries at RF frequencies of **900 MHz** (e.g., GSM mobile phones and base stations, baby monitors, cordless phones, headphones, smart meters), **1.8 GHz** (e.g., GSM, cordless phones), **2.1 GHz** (UMTS mobile phones and base stations), and **2.45 GHz** (e.g., microwave oven, baby monitors, Bluetooth, home area network).

Table 2. RF exposure limits for the general public in different countries
Equivalent plane wave power density, **W/m²**

FREQUENCY / COUNTRY	900 MHz	1.8 GHz	2.1 GHz	2.45 GHz
ICNIRP	4.5	9	10	10
Canada	6	10	10	10
USA	6	10	10	10
Japan	6	10	10	10
Australia	4.5	9	10	10
Austria	4.5	9	10	10
Belgium	4.5	9	10	10
Finland	4.5	9	10	10
France	4.5	9	10	10
Germany	4.5	9	10	10
UK	4.5	9	10	10
Spain	4.5	9	10	10
Ireland	4.5	9	10	10
Bulgaria	0.10	0.10	0.10	0.10
Poland	0.10	0.10	0.10	0.10
Russia	0.10	0.10	0.10	0.10
Switzerland	0.045	0.095	0.095	0.095

Most Western European countries apply ICNIRP's RF limits. Some Eastern Europe countries like Russia, Poland, and Bulgaria have adopted more stringent limits of the order of 2% of ICNIRP reference levels, but it is unclear how they are enforced.

The RF exposure limits adopted in Canada and the USA are similar to ICNIRP reference levels, except at 900 MHz.

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Section 14

Strategies for Radiofrequency Exposure Reduction

Table of Contents

Summary

- Although there is no clear evidence of health effects related to public exposure to radiofrequency (RF) fields, strategies exist to reduce personal exposure to RF.
- The mitigation strategies can include substitution, engineering controls, and administrative controls.
- With substitution, one can replace certain wireless RF devices with hard-wired alternatives, e.g., substituting landline corded phones for mobile phones and cordless phones.
- Engineering controls include choosing devices that emit lower RF levels. Some devices have engineering modifications, like power-saving and non-idling functions.
- Administrative controls include limiting duration and frequency of use as well as turning off devices, where possible, when not in use. In general, distancing from RF-emitting devices will reduce personal exposure. For mobile phones, options are the use of headsets, the speaker phone and text-messaging.
- Attempts at shielding from RF are typically ineffective and may actually enhance exposure.

14.1 Introduction

The increasing use of RF devices for communication has provided benefits of convenience, practicality, and innovation to society as a whole. Use of mobile phones has promoted safety and saved countless lives by allowing remote communication. Furthermore, the scientific evidence to date offers no clear evidence of health effects associated with public exposure to RF.[1-3] However, mitigation strategies do provide an option for the concerned public to reduce personal exposures to RF. As there are multiple sources of RF, reducing or eliminating one source may have limited impact on total personal exposure to RF, and possibly very little impact on exposure to EMF in general.

In occupational hygiene, the hierarchy for exposure reduction includes substitution, engineering controls, administrative controls, and personal protective equipment. In the case of reducing RF exposure to the general public, similar strategies include non-use, technology and design changes for RF-emitting devices, distancing and limiting use, and exploration of shielding measures.

14.1.1 Substitution

The most effective way to reduce total exposure to RF is to avoid the use of RF-emitting devices, especially devices that result in the highest personal exposures such as mobile phones used at the head. Exposure to RF from mobile phones or cordless

phones can be eliminated by using landline corded phones but with loss of flexibility in communication. Direct cable connections can replace use of a wireless local area network (WLAN) or WiFi, but the effective reduction to total RF is minimal.[4] As well, improperly wired connections, which are not uncommon, can produce magnetic fields.[5]

14.1.2 Engineering controls

The next most effective method of exposure reduction is to use devices that produce lower output power and specific absorption rates (SAR).

It is possible to choose mobile phones with a lower US Federal Communications Commission (FCC) rating of SAR (tested at maximum power). However, a lower SAR FCC rating does not necessarily translate into lower real-world SAR as contemporary mobile phones do not often reach or maintain maximum output power levels in the field.[6] The published literature indicates that, compared to Global System Mobile (GSM) second generation (2G) mobile phones, the technologies of Code Division Multiple Access (CDMA) (2G) and third-generation (3G) wide-band CDMA (wCDMA) and Universal Mobile Telephone System (UMTS) produce lower RF power measurements by not transmitting as often at maximum power.[6] More research is needed to assess the newer technologies associated with fourth generation mobile phones using Long Term Evolution (LTE) or Worldwide Interoperability for Microwave Access (WiMax) to determine what RF output power levels they produce in real-world situations.

Engineering features used to mitigate RF exposure from mobile phones include power control, discontinuous transmission, increased efficiency (requiring lower power output) and improved antenna placement. Good base station coverage will minimize RF exposure when using a mobile phone, as adaptive or power control reduces the output power to the minimum necessary for fidelity of the signal.[7] Living further away from base stations (e.g., in a rural area with poor base station coverage), does not necessarily decrease overall exposure for mobile phone users, as the mobile phone needs to increase output power levels to maintain a good connection. In general, choosing devices that operate at higher frequencies may reduce absorption of RF into tissues.[1] RF exposure from cordless phones can be reduced by choosing ones that have the following features: 1) a power-saving function (which allows for a decrease in output power when the connection is good, and 2) a system that does not intermittently signal (send a beacon) when the handset is off and placed in the cradle of the base station.[8]

Many RF-emitting devices have already incorporated engineered features that mitigate scatter and exposure. Smart meters have very low duty cycles, transmitting RF only for milliseconds, which limit active exposure to RF. As well, they have back plates that significantly reduce RF transmission into the house (as does the house wall to which they are attached). Because banks of smart meters need to communicate with a single controller, only one smart meter can communicate at a time, which eliminates the possibility of exposure to multiple signals simultaneously.[9]

14.1.3 Administrative controls

Exposures are highest in the near field of RF-emitting devices (e.g., several centimetres for most mobile phones [depending upon the antenna size] and 16–33 cm for WLAN access points [wireless routers]).[10,11] In the far field, the power density decreases proportionally to the square of the distance between the emitter and receiver, therefore exposures become minimal in the far field.[12]

For mobile phones, distancing can be accomplished through use of headsets, use of the speaker phone, or text-messaging while keeping the phone away from the body/head. Studies show that SAR measurements at the head are 8–20 times lower when using a wired hands-free kit than when using the phone at the ear.[13] However, one study indicated although wired hands-free kits decreased overall SAR at the head, they could increase localized SAR in the region of the ear due to the increased magnetic field exposure from the wired ear phone.[14] Two Bluetooth headsets were tested for the Swiss Federal Office of Public Health (FOPH) and the SAR values were 12 and 34 times lower than the SAR for the lowest-emission mobile phone available.[8] For cordless phones, headsets and speaker functions can also be used.

Although not using the phone next to the head may reduce exposure, it can result in increased exposure to specific areas of the body and it can also reduce the efficiency of the phone if the body impedes the signal, causing increased output power and exposure to RF. As power output for data transfer, such as downloading files from the internet, can be up to four to 30 times higher than voice data transfer (depending on the technology), distancing the device from the body while transferring data can decrease exposure.[6,8]

Even when not in use but powered on, mobile phones continue to emit RF, albeit at low levels. To limit this type of exposure, mobile phones can be kept away from body areas when in use (i.e., not on belts or in pant pockets). Because the mobile phone is attempting to maintain connection even when not in active use, shutting off the phone will limit exposure to low levels of RF. For GSM phones, the first connection to the base station occurs at maximum power before dropping to a lower output power level; therefore, turning on and off the phone frequently could increase overall exposure.[15] Limiting duration of use, such as the length of a mobile phone call, and number of calls, will also reduce personal exposures.

Far-field WiFi emissions of RF are much lower than for near-field RF when using mobile phones at the head. Although WLAN access points can be placed far from WLAN terminal devices, this can result in a poor connection, thus increasing output power. While a laptop computer with WIFI capabilities directs RF across the screen and up away from the body,[10] which limits exposure to RF, using a laptop computer on a table at some distance from the body can further reduce other EMF exposures. Because WLAN continues to transmit intermittently (but at very low levels of RF) to continue establishing a connection even when not in active use, devices can be shut off when not in use.

For mobile phone base stations, distance does not necessarily translate into lower exposures to RF. The direction of the radiated power (main lobe) is also an important determinant of level of exposure that is better indicated by line-of-sight. For instance, in a Bavarian study, buildings or vegetation blocking direct sight to a base station reduced power density to 1/30th of the levels compared to points with sight to the base station, but at the same distance.[7]

14.1.4 Protective equipment

Source shields or protective devices have limited effectiveness in reducing exposure at the cost of interfering with the signal. Shielding from base stations requires creation of a complete metallic cage, but even a small opening or a slit may reduce the shielding effect substantially. In addition, a shield to reduce ambient levels of RF may cause any RF-emitting sources indoors (e.g., mobile phones or cordless phones) to generate resonances producing higher local exposures when using that particular device than without shielding.[7]

Shields for mobile phones are available, but when tested, earpiece pads and shields did not affect SAR substantially, sometimes decreasing SAR marginally but sometimes increasing it.[16] Antenna caps did reduce SAR up to 99%, but they also deteriorated the signal quality. Some shielded cases reduced the SAR without impairing signal quality, whereas others reduced signal quality corresponding to the reduction in SAR. Another problem with using shielding of mobile phones is that it reduces the battery life.[8] For the most part, tests on mobile phone protectors demonstrate that these are either ineffective or increase the transmit power to compensate for the interference with the signal.[7] No evidence could be found that suggests metallic clothing or headgear reduces exposure to ambient RF.

Table I provides a summary of mitigation strategies as suggested by national and international public health organizations, grouped according to the hierarchy of occupational hygiene exposure reduction methods. The specific recommendations for exposure reduction to RF by the World Health Organization as well as Canadian, US, and other international organizations are given in Appendix A.

Table 1. Mitigation strategies for reducing personal exposure to RF

RF Source	Substitution	Engineering Controls[8]	Administrative Controls[8]	Protective Equipment
Mobile phone	Limit use Use landline phones	Use phones with low SAR ratings Use phones that emit at lower output power in the real-world scenarios	Keep phone at a distance from the head using handsets or speaker phone function Do not place in front of pocket or against body during use or when left on Limit duration of use Only use when connection with base station is good	Do not use shields
Cordless phones	Use landline phones	Use models with a power-saving function that decreases output power when the connection is good Use models that do not produce beacon signals when placed in the base- station cradle	For some models, store the handset in base station cradle For some models, ensure base station maintains good connection with phone Keep phone base station at least 50 cm from area of use	Do not use shields
WLAN	Limit use Use wired systems	Only use the antenna provided with the WLAN transmitter	Install access point at least 1 m away from work area Position access point in central location so all devices have a good connection Do not hold device against body when in use Turn off WiFi when not in use	Do not use shields

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14.3 Appendices

Appendix A: Statements regarding reduction of exposures by International Organizations

World Health Organization (WHO)

WHO established the International Electromagnetic Fields (EMF) Project[17] in 1996 to assess the scientific evidence of possible adverse health effects from electromagnetic fields. WHO will conduct a formal risk assessment of all studied health outcomes from radiofrequency fields exposure by 2012. In a factsheet on EMF and health effects, the WHO notes that “using "hands-free" devices, which keep mobile phones away from the head and body during phone calls, exposure is also reduced by limiting the number and length of calls. Using the phone in areas of good reception also decreases exposure as it allows the phone to transmit at reduced power. The use of commercial devices for reducing radiofrequency field exposure has not been shown to be effective.”[2]

Canada

The Health Canada website provides these strategies for reducing RF exposures from mobile phones: 1) limit the length of cell phone calls, 2) use "hands-free" devices, and 3) replace cell phone calls with text messages. Health Canada also encourages parents to take these measures to reduce their children's RF exposure from mobile phones since children are typically more sensitive to a variety of environmental agents. Health Canada also does not recommend any precautions to limit exposure to RF energy from mobile phone towers as exposure levels are typically well below those specified in health-based exposure standards.[18]

United States

The US Environmental Protection Agency (EPA) indicates on their website that “although there is not sufficient evidence to conclude that there is a definite risk associated with long-term mobile phone use, people who are concerned can take simple steps to reduce exposure: 1) Limit use – reducing the number/length of calls, 2) Use "hands-free" devices – Using “hands-free” devices can help to keep mobile phones away from the head.”[19]

Europe

UK’s Health Protection Agency says, "Measures that could be taken to reduce exposures were described in the IEGMP report and in the subsequent Mobile Phones and Health 2004 report [6], but the technology continues to develop, which alters the options available. Moving the phone away from the body, as when texting, results in very much lower exposures than if a phone is held to the head. Also, the use of the more recent 3G mode of transmission instead of the older 2G mode will produce much

lower exposures. Other options to reduce exposure include using hands-free kits, keeping calls short, making calls where the network signals are strong, and choosing a phone with a low specific energy absorption rate (SAR) value quoted by the manufacturer. Exposures from devices held further away from the body such as wireless-enabled laptop computers, and transmitter masts in the community are very much lower than those from mobile phones and community or individual measures to reduce exposures are not necessary."
http://www.hpa.org.uk/Publications/Radiation/HPAResponseStatementsOnRadiationTopics/radresp_AGNIR2012/[20]

The Norwegian Institute of Public Health mentions that 1) hands-free mobile phones reduce exposure significantly, 2) when a GSM mobile phone transmits at maximum power, exposure from some models may exceed ICNIRP's reference values, 3) greater density base station density leads to lower exposures, 4) technological advancements of mobile phones is decreasing exposure and that although mobile phone use may be increasing, the exposures may be decreasing due to the fact that newer UMTS phones produce much lower power than GSM.[21]

The Federal Office of Public Health (FOPH) in Switzerland offers the most detailed and prolific recommendations for minimizing exposure to RF[8]:

Mobile phones

1) For new phone purchases, ensure the phone has low SAR.
2) Keep calls short and use text-messaging.
3) Use hands-free system (headphone, headset) with low power Bluetooth emitter.
4) Whenever possible, ensure signal quality is good.

FOPH provides further advice such as warning against the use of shielding devices which may make connection quality worse, thereby increasing output power.[8] Also, FOPH recommends keeping mobile phones at least 30 cm from active medical implants.[8]

Cordless (DECT) phones

1) Ensure DECT base units are at least 50 cm from relaxation places or work stations occupied for long periods.
2) For longer calls, used corded phones or headset.
3) Low radiation DECT phones are available in some facilities. Models are available where the base station does not emit radiation when the handset is in place and where the headset reduces output power if the connection is good.

Bluetooth

Some mobile phones that use Bluetooth to access the internet use Class 1 transmitters which transmit at similar levels to a mobile phone. FOPH recommends that for that the internet connection is switched off when making phone calls to reduce exposure to the head.

WLAN

1) Only switch on WLAN when needed.
2) Don't hold your laptop close to the body while it is connected to WLAN.
3) Whenever possible, install the WLAN access point 1 m from places where you work, sit or rest for long periods of time.
4) Position access point centrally so that all the devices have good reception.
5) Choose WLAN g standard over b standard. Exposure is lower because it transmits data more efficiently.
6) WLAN transmitter must only be used with an antenna provided for this purpose by the manufacturer. If an unsuitable antenna is used, the maximum permitted transmission power may be exceeded.

Microwave ovens

FOPH makes recommendations around safety and handling of foods in microwaves, but the only recommendation related to RF is to keep the door frame and seal clean and check that the door latch and seal is intact. However, based on testing of a microwave oven with the maximum permitted leakage radiation allowed (5 mW/cm^2 at 5 cm), FOPH reports that the recommended threshold was exceeded only with direct contact with the microwave oven; at 5 cm, levels were much lower than SAR limits.

Baby monitors

1) Place baby monitor at least a metre away from crib.
2) Do not use systems that transmit continuously. Set the baby unit to voice activation mode.
3) Ensure that the adaptor is plugged in at least 50 cm away from the crib.

Section 15

Overview of Major Ongoing Research Projects on Electromagnetic Fields and Health

Table of Contents

Research studies on potential health effects due to exposure to electromagnetic fields (EMF) have been conducted for at least 30 years in several parts of the world. Many projects have been initiated by international organisations, universities, research institutions, and specialized centers.

In this section of the toolkit, six important ongoing international projects on electromagnetic fields and health are presented:

1. The EMF project of the World Health Organization (WHO)
2. MOBI-KIDS project: Study on Communication Technology, Environment and Brain Tumours in Young People
3. EFHRAN: European Health Risk Assessment Network on Electromagnetic Fields Exposure
4. COSMOS project: Cohort Study of Mobile Phone Use and Health.
5. SEAWIND project: Sound exposure and risk assessment of wireless network devices
6. NTP Rodent project: National Toxicology Program laboratory multigenerational rodent studies.

15.1 The EMF Project of the World Health Organization[1]

The International Electromagnetic (EMF) project was established by the World Health Organization (WHO) in 1996. Participants in the project include several countries, the International Commission on Non-Ionizing Radiation Protection (ICNIRP), and WHO collaborating institutions from Australia, Canada, Germany, UK, and the US. Canada is represented in this project by the University of Ottawa.

The project was initiated because of scientific questions and public concerns regarding potential health effects of electromagnetic emissions in the frequency range 0 Hz–300 GHz. It includes four themes: (1) scientific research, (2) development of databases for researchers worldwide, (3) guidance for the development of EMF safety standards, and (4) transfer of knowledge.

The project defined two distinct areas to be investigated:

- At extremely low frequencies (ELF), the project is focused on the risk of leukemia among children exposed to 50/60 Hz magnetic fields from electrical power lines. This subject was considered important because of previous epidemiological studies suggesting that children exposed to ELF magnetic fields may be at increased risk of developing leukemia.
- In the RF range of the electromagnetic spectrum, i.e., from 100 kHz to 300 GHz, the fast development of mobile phone technology and its extensive use among

children and young adults raised concerns about the potential impact of RF waves from mobile phone radiating antennas on a user's head, considering the very short distance between the antenna and the head.

- The number of mobile phone users is expected to continue increasing, particularly among children and teen age populations.

As a result, for EMF in the radiofrequency range, the aim of the research is to study the potential long-term health effects associated with mobile phone use.

The research program of the EMF project is overseen by an ad hoc Research Coordination Committee (RCC) composed of specialists representing national and international institutions.

EMF project progress reports

To date, 16 progress reports (1997–2011) have been posted on the WHO website: http://www.who.int/peh-emf/publications/reports/en/index.html

The 2012 report has not yet been released.

15.2 MOBI-KIDS Project[2]

The MOBI-KIDS project is an international case-control study on potential risks of brain cancer among young mobile phone users. It was initiated in 2009 and involves 16 research centers from European and non-European countries including Canada, which is represented by the University of Ottawa in this project. Invitations to join the research program have been extended to other countries as well.

The main objective of the project is to assess the potential association between mobile phone use and brain tumours in young individuals aged 10 to 24 years.

Over the period 2010–2014, the epidemiological study will involve two groups of mobile phone users: 2000 young people with brain tumours and a similar number without brain tumours.

A basic project questionnaire is used by the participating centres to collect information about the two groups. The questionnaire includes questions on demographic factors, residential history and mobile phone use habits.

In addition to the data collected by participant centres, RF exposure evaluations will be performed by two European centres known for their technical capability in the field.

Some complex issues in this project need to be considered. First, brain tumours among young people are not frequent and may have different causes, i.e., environmental factors other than RF, genetic reasons, etc. Secondly, the projected number of 2000 young people affected by this malignancy might not be easy to reach and may not be large enough to draw precise estimates of risk. Further, the

intermittent exposures to RF waves from mobile phone antennas are considered too low in comparison to ICNIRP's exposure limits and unlikely to induce brain malignancies.

Nevertheless, it is believed that a larger participation of countries at the world level to increase significantly the study sample may help in detecting any possible association between mobile phone use and brain cancer if such an association exists.

MOBI- KIDS project progress reports

No progress report has been released so far. The University of Ottawa, which is the Canadian participant in this project, will be requested to provide any useful information about the advancement of this project.

15.3 European Health Risk Assessment Network on Electromagnetic Fields Exposure (EFHRAN)[3]

The European Health Risk Assessment Network on Electromagnetic Fields Exposure (EFHRAN) is a three-year (2009–2011) project funded by the European Commission (EC) aiming at establishing a network of experts to conduct health risk assessments for exposure to EMF waves. Participants include universities, research centres and collaborating partners from the European Union along with a few non-European countries and WHO.

The project covers low frequency (0–300 Hz), intermediate frequency (300 Hz–100 kHz), and high frequency (100 kHz–300 GHz) electromagnetic waves. This overview will focus on RF waves.

The main research goals of the project are: monitoring evidence of EMF-related health risks and quantification of potential health risks posed by EMF.

Three research areas were defined in the EFHRAN project:

- Exposure and dose assessment
- Risk analysis and hazard identification
- Risk characterization and management.

Only the research part of the project, i.e., exposure and dose assessment, will be discussed in this section.

Exposure and dose assessment

This part is related to the evaluation of the EMF exposure levels in Europe for RF waves and Extremely Low Frequency (ELF) EMF fields. Several methods were used to investigate the levels and patterns of public exposure to RF in some European countries and the main ones are described below:

a. Permanent RF monitoring systems: Survey programs have been conducted by means of continuous RF monitoring systems to record emissions from fixed RF sources such as radio and television stations, mobile phone base stations, radars, etc. Such systems have been installed in Italy, Greece, Germany, Portugal, Malta, Slovenia, and the UK. The readings recorded by the monitoring systems are accessible to the general public through internet gateways.

b. On-site RF measurement campaigns: These are measurements that have been conducted near mobile phone base stations in nearly all European countries since the 1990s. The results of the surveys showed that more than **60%** of the measured RF exposures were below 0.003 W/m^2; fewer than **1%** were above 0.095 W/m^2; and fewer than **0.1 %** were above 1 W/m^2.

   The recommended public exposure limits in European countries range from 4 to 10 W/m^2.

c. Personal and micro-environmental RF exposure assessment: In this study, a selected number of individuals from the general public were provided with personal exposure meters (PEM) to wear during several days for the assessment of their exposure.

   The results of the experiment showed that the average personal exposures were far lower than the on-site exposures (point b).

d. Exposure from mobile phones: Europe has the highest penetration of mobile phone use in the world. The assessment of mobile phone exposure was conducted on the basis of different studies carried out in Europe and outside the continent. It was concluded that the local exposure in the head due to mobile phone use is considerably higher than that due to other RF sources such as broadcast stations and mobile phone base stations.

e. Exposure to RF wireless systems: The studies that were conducted in some European countries showed that the exposure to wireless devices such as cordless phones, blue tooth, and Wi-Fi systems were below mobile phone exposure. However, for long periods of exposure to wireless sources, the total exposure due to wireless systems may not be negligible.

In addition to the above assessments, the project provides useful information on RF dosimetry modelization and RF dosimetric considerations of far field exposure.

To summarize this part on exposure assessment, it is established that mobile phones and portable wireless devices contribute the most to the exposure of the public.

EFHRAN project progress reports

The following reports have been released by EFHRAN:

- Risk analysis of human exposure to electromagnetic fields (revised) – October 2012[4]
- Report on the level of exposure (frequency, patterns, and modulation) in the European Union – Part 1: Radiofrequency (RF) radiation (Aug. 2010)[5]
- Risk analysis of human exposure to electromagnetic fields ((July 2010)[6]
- Report on the analysis of risks associated to exposure to EMF: in vitro and in vivo (animals) studies (July 2010).[7]

15.4 COSMOS Project[8]

COSMOS is a recent project launched by six European countries: Denmark, Finland, France, Netherlands, Sweden, and the UK. Additional European countries are invited to join the COSMOS program.

It is a cohort study investigating possible health effects from long-term use of mobile phones and other wireless technologies.

The health of approximately 250,000 European mobile phone users forming the cohort will be followed. The duration of the monitoring is not mentioned, but it is probably longer than 12 years, as recommended by some European health agencies since short term exposure studies (10 years or less) are no longer considered suitable.

The health effects to be studied include:

- Changes in the frequency of specific symptoms over time, such as headaches and sleep disorders
- Risks of cancers and benign tumours
- Neurological and cerebrovascular diseases.

COSMOS project progress reports

No progress report has been released so far as this is a recent project. A paper on project design and enrolment was published in 2011[9]:

Schüz J, Elliott P, Auvinen A, Kromhout H, Poulsen AH, Johansen C, Olsen JH, Hillert L, Feychting M, Fremling K, Toledano M, Heinävaara S, Slottje P, Vermeulen R, Ahlbom A. **An international prospective cohort study of mobile phone users and health (Cosmos): design considerations and enrollment. Cancer Epidemiol. 2011 Feb; 35(1):37-43.**

15.5. SEAWIND project[10]

SEAWIND, Sound Exposure and Risk Assessment of Wireless Network Devices, is a 3-year project funded by the European Union, starting Dec. 2009, on exposure of the population to wireless RF devices and their potential health effects. Forty scientists from eight research institutions in Europe participate to the project.

The RF devices of interest in the project include various consumer devices including: cell phones, cell phone base stations, broadcasting stations, wireless networks (WLAN, WMAN, WiMax, WPAN), cordless phones, RFID scanners, baby monitors, and Bluetooth devices.

The objectives of SEAWIND are to:

- Conduct measurements of public exposure
- Determine fields induced inside the body
- Assessthe effect of RF exposure on cells and DNA
- Use the findings of the project to assist policymakers.

SEAWIND progress reports

As of now, only one report, entitled "Literature review of exposure assessment and dosimetry of wireless network" is available.[11] The report includes useful information and details related to the theoretical and experimental methods applied to assess exposure of members of the public to RF devices. The conclusions of the research report include the following:

- The exposure of the public to all kinds of wireless devices is, in general, well below the ICNIRP reference levels at all frequencies
- Continuous monitoring indicates that the exposure in urban areas is greater than in rural areas
- Personal exposure meters (PEM) data should be used with caution due to technical specifications and should not be employed to evaluate exposure from wireless devices used by the individual wearing the device
- Cell phones deliver the highest exposure (SAR) to the population but Radiofrequency Identification (RFID) Readers (e.g. used for toll booth passes or smart cards) may exceed the exposure to cell phones if in contact with the body
- Indoor exposure to RF and use of new wireless devices requires more research because of scarcity of data in the literature
- Foetal exposure to RF due to the mother's use of wireless devices during pregnancy should be investigated further.

15.6 National Toxicology Program (NTP) Rodent Project[12]

The National Toxicology Program (NTP) headquartered at the U.S. National Institute of Environmental Health Science is conducting laboratory multigenerational rodent studies on the effects of exposure to mobile phone radiofrequency. The studies are being carried out with both sexes of rats and mice and with pregnant female rats. The NTP studies are designed to mimic human exposure and are based on the frequencies (900 and 1900 Mhz) and modulations (CDMA and GSM) in use in the United States.

The NTP has worked closely with radiofrequency experts from the National Institute of Standards and Technology to design a highly specialized exposure system to provide uniform exposure to RF to unrestrained rodents. After establishing field strengths that do not excessively raise body temperature, they are conducting a series of toxicology and carcinogenicity studies.

NTP rodent project progress reports

No progress reports are available. The chronic toxicology and carcinogenicity studies were anticipated to be completed in late 2012 with final study results expected in 2014.

15.7 References

1. World Health Organization. The international EMF project. Geneva, Switzerland: WHO; [cited 2012 Oct 16];
Available from: http://www.who.int/peh-emf/project/en/

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Available from: http://www.mbkds.net/

3. EFHRAN - European Health Risk Assessment Network on EMF exposure. Welcome to EFHRAN. Milan, Italy: European Health Risk Assessment Network on Electromagnetic Fields Exposure; 2010 [updated Aug];
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Available from: http://efhran.polimi.it/dissemination.html

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Available from: http://efhran.polimi.it/docs/IMS-EFHRAN_09072010.pdf

8. COSMOS - Cohort Study of Mobile Phone Use and Health. About us. London, UK: UK Department of Health; 2012;
Available from: http://www.ukcosmos.org/aboutus_3.html

9. Schüz J, Elliott P, Auvinen A, Kromhout H, Poulsen AH, Johansen C, et al. An international prospective cohort study of mobile phone users and health (Cosmos): design considerations and enrolment. Cancer Epidemiol. 2011;35(1):37-43.

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12. National Institute of Environmental Health Sciences. Cell phones. Research Triangle Park, NC: NIEHS; [updated 2013 Apr 1]; Available from: http://www.niehs.nih.gov/health/topics/agents/cellphones/

Section 16

International Reports on Radiofrequency Exposures and Health Effects

Table of Contents

Several recent comprehensive reports review the published scientific literature concerning exposure to radiofrequency (RF) and electromagnetic fields (EMF) and the associated biological and health effects. In this section, reference is made to eight recent international reports (listed in alphabetical order) along with a brief description of their contents and citation to access the reports online.

16.1 Advisory Group on Non-Ionizing Radiation (AGNIR, UK)

Health Effects from Radiofrequency Electromagnetic Fields.

Report of the Independent Advisory Group on Non-ionising Radiation.

Documents of the Health Protection Agency, April 2012.

Chairman: Professor AJ Swerdlow, Institute of Cancer Research, University of London

Citation: Health Protection Agency. Advisory Group on Non-ionising Radiation (AGNIR). London, UK.

Available from:
http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1317133826368

The AGNIR became an independent advisory group in 1999 and published a review in 2003 of the health effects of RF EMF. This update (324 pages) concentrates on new scientific evidence published since 1993, up to early 2011.

The review evaluates individual human and epidemiological studies, with the exposure and health content of the review organized as follows:

Ch 2 Exposures, characteristics of RF fields, interaction mechanisms between RF fields and the body, dosimetry and sources of exposure to RF fields

Ch 3 Cellular studies on genotoxic effects, gene expression, and potential mechanisms leading to carcinogenesis

Ch 4 Experimental studies of RF effects using animal models of brain and nervous system function, behaviour, endocrine and auditory effects, immunology, reproduction and cancer assays.

Ch 5 Acute cognitive and neurophysiological effects from mobile phone use as determined by provocation and observation studies

Ch 6 Effects on symptoms, as evaluated by experimental and observational studies, and the issue of hypersensitivity to RF fields

Ch 7 Possible reproductive effects from exposure to RF fields, including fertility, sexual function, birth outcomes and child development, in addition to cardiovascular function

Ch 8 Cancer risks, emphasizing brain tumours and acoustic neuromas in relation to mobile phone use as well as cancers (primarily leukemia) associated with residence near RF transmitters and lymphoma with certain occupations

16.2 BioInitiative Report

Citation: BioInitiative Working Group, Cindy Sage and David O. Carpenter, Editors.

BioInitiative Report: a rationale for a biologically-based public exposure standard for electromagnetic radiation.

Available from:
http://www.bioinitiative.org/report/wp-content/uploads/pdfs/BioInitiativeReport2012.pdf

This large report (1,484 pages) includes original chapters from the 2007 BioInitiative report (Blackman CF, Blank M, Kundi M, Sage C, Carpenter DO, et al. BioInitiative report: a rationale for a biologically-based public exposure standard for electromagnetic fields) accompanied by a 2012 supplement of newer studies. The purpose of the report is to update evidence from science, public health, and public policy over the past five years regarding the health issues pertaining to exposure to EMF and RF.

The first four sections by Cindy Sage provide an overview, a statement of the problem, existing public exposure standards and evaluation of their adequacies for managing ELF and RF. For RF, sections on biological effects include evidence of gene and protein expression (transcriptomic and proteomic research), genotoxic effects, response by stress proteins, and immune function. Effects on neurologic function and behaviour include a comprehensive review of studies on cellular changes, animals, electrophysiology, cognitive function, auditory effects and human subjective effects.

Separate sections include the effects on the blood-brain barrier and evaluating epidemiological studies of brain tumours and acoustic neuromas (authored by Dr. Lennart Hardell and colleagues). The aim of the final chapter is to provide an overview of the complex dependence of non-thermal microwave effects on various biological and physical parameters (e.g., bandwidth, frequency, modulation, and polarization). Reproductive health effects and fertility are discussed as are fetal and neonatal effects. Studies evaluating a possible link to autism are reviewed. The final three sections relate to precautions and public health policy recommendations.

16.3 EFHRAN – European Health Risk Assessment Network on EMF Exposure

Citation: EFHRAN – European Health Risk Assessment Network on EMF exposure. Risk analysis of human exposure to electromagnetic fields (revised).

Milan, Italy: European Health Risk Assessment Network on Electromagnetic Fields Exposure; 2012 Oct.

Available from: http://efhran.polimi.it/docs/D2_Finalversion_oct2012.pdf

EFHRAN was funded by the European Commission to establish a network of experts from seven European countries. The purpose was to develop a risk assessment network on low, intermediate, and high frequency EMF and health issues. For the section on high frequencies (RF), current consensus of opinions are followed by evidence from more recent epidemiological and experimental studies, followed by a discussion of interaction mechanisms. A four-point rating of the evidence of specific health risks associated with exposures to RF is provided: a) sufficient; b) limited; c) inadequate; and d) evidence suggesting a lack of effects.

16.4 International Commission on Non-Ionizing Radiation Protection (ICNIRP)

Citation: Vecchia P, Matthes R, Ziegelberger G, Lin J, Saunders R, Swerdlow A, Editors. Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz–300 GHz). Oberschleissheim, Germany: International Commission on Non-Ionizing Radiation Protection (ICNIRP); 2009.

Available from: http://www.icnirp.de/documents/RFReview.pdf

Each chapter of this 354-page report is written by a group of authors active in the field. The major topics include (1) dosimetry of high frequency electromagnetic fields; (2) review of experimental studies of RF biological effects (100 kHz–300 GHz) and (3) epidemiological evidence on the health effects of RF exposure and on tumour risks from mobile phones.

The content of each section includes:

(1) Physical characteristics, sources and exposures, RF measurement, mechanism of interaction of RF exposure and biological systems, and dosimetry, including SAR.

(2) Biological evidence for interaction mechanisms, cellular studies (genotoxic efects), animal studies (cancer, reproduction, nervous, auditory and cardiovascular systems, immunology and eye and skin tissues); human studies (nervous, endocrine and cardiovascular systems).

(3) Epidemiology, with sections on exposure, mechanisms, outcomes, occupational exposures, environmental exposure from transmitters and on mobile phone use. A separate section reviews epidemiological evidence on mobile phones and risk of tumours, with consideration of exposure, laterality of tumour and recall of phone use, induction and latency period, case and control considerations, response rates and precision of risk estimates. Results and interpretation are provided for studies on RF effects on the head and neck tumours of glioma, meningioma, acoustic neuroma, and of the salivary gland.

16.5 Latin American Experts Committee on High Frequency Electromagnetic Fields and Human Health

Citation: Latin American Experts Committee on High Frequency Electromagnetic Fields and Human Health. Non-ionizing electromagnetic radiation in the radiofrequency spectrum and its effects on human health.

Campinas/SP, Brasil: Instituto Edumed – Edumed Institute for Education in Medicine and Health Independent Research Group on the Impacts of Mobile Technologies on Health; 2010 Jun.

Available from:
http://www.wireless-health.org.br/downloads/LatinAmericanScienceReviewReport.pdf

The literature review examines the scientific evidence for possible biological and health effects of RF, due to exposures relevant to base stations or use of mobile phones, as follows:

- Biological effects covered include changes in cell cycle and regulation, membrane transport, apoptosis, genotoxicity, mutation rates, gene and protein expression, as well as damage to genetic material including cell proliferation, transformation, and differentiation of cells and tissues.
- In vivo animal studies include evaluation of the disruption of the blood-brain barrier and the induction and promotion of tumours or blood neoplasms.
- Human provocation studies cover possible effects on the nervous system, including many cognitive and behavioural responses, in response to low-level RF fields emitted by mobile telephones near children, as well as in adults. Other effects considered are pain, vision, hearing and vestibular function, as well as endocrine and cardiovascular system function.
- Epidemiological observational studies include assessment of community exposures and health complaints due to base stations antennas. The majority of the epidemiological studies covered investigate possible effects of RF exposure of mobile phone handset users. The principal outcomes considered are malignant and benign tumours of the nervous system, especially gliomas and acoustic neuromas.
- Other epidemiological studies relate exposure of populations to RF from mobile phones or base stations to several other health problems such as neurodegenerative disorders, cardiovascular diseases, cataracts, reproductive health changes, behavioural changes and nonspecific symptoms including “RF hypersensitivity symptoms.”

16.6 Norwegian Institute of Health Expert Committee

Citation: Norwegian Institute of Health Expert Committee. Report 2012:3 Low level radiofrequency electromagnetic fields – an assessment of health risks and evaluation of regulatory practice. Norway; 2012

Available from: http://www.fhi.no/dokumenter/545eea7147.pdf

The mandate for the Expert Committee, formed in 2010, was to summarise the knowledge regarding exposure and potential health effects related to weak RF fields particularly from mobile masts, base stations, and wireless networks. In addition to consideration of the suitability of threshold limit values, an assessment was undertaken of how the potential risks related to exposure from electromagnetic fields should be managed in Norway.

Part I assesses current exposure to RF fields, summarizes knowledge of potential health hazards including cancer, reproductive health and nervous system effects and provides a risk assessment

Part II addresses the general health problems attributed to EMF (electromagnetic hypersensitivity)

Part III describes risk management, risk perception, and concern for harmful effects of RF fields

Part IV reviews the present regulations of RF fields in other countries, as well as in Norway

Part V assesses the current regulations in Norway and offers recommendations on regulating public exposure to RF fields

16.7 Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

Citation: Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Health effects of exposure to EMF. Brussels, Belgium: European Commission; 2009.

Available from:
http://ec.europa.eu/health/archive/ph_risk/committees/04_scenihr/docs/scenihr_o_022.pdf

This report (44 pages) from the European Commission updates the SCENIHR opinion (March 2007) on the health effects of exposure to EMF and includes guidelines for assessing recent published evidence.

For RF, the sections include sources of exposure and their distribution, a section on dosimetric aspects of children's exposure and reviews of health effects, including

sections on the epidemiology and in vivo and in vitro cancer studies, symptoms, nervous system effects, and reproduction and development.

The section on methodological frameworks presents the criteria for how studies were selected and how the scientific evidence was synthesised into an assessment of the evidence for a causal effect of exposure to EMF and health effects. The section includes consideration of dosimetry and exposure assessment, epidemiology, and human laboratory studies, as well as in vivo and in vitro studies.

16.8 Swedish Radiation Safety Authority

Citation: SSM:s Independent Expert Group on Electromagnetic Fields. Recent research on EMF and health risk. Seventh annual report. Stockholm, Sweden: Swedish Radiation Safety Authority; 2010 Dec.

Available from:
http://www.stralsakerhetsmyndigheten.se/Global/Publikationer/Rapport/Stralskydd/2010/SSM-Rapport-2010-44.pdf

The SSM report (44 pages) summarizes the recent literature on Extremely Low Frequency (ELF) fields and RF fields according to cell, animal, human laboratory, and epidemiological studies.

The experimental studies reviewed on RF include cell studies (with endpoints of DNA damage, production of reactive oxygen species (ROS), gene expression and effects on spermatozoa); animal studies; human laboratory studies (including EEG, sleep, cognition and symptoms, and epidemiological studies on mobile phone use, with emphasis on the INTERPHONE study); and transmitter studies, including reproductive effects.

List of selected recent international reviews on studies of biological and health effects associated with exposure to RF-EMF:

- Health Protection Agency. Advisory Group on Non-ionising Radiation (AGNIR). London, UK: HPA; [updated May 11, 2012; cited 2012 Oct 16]; Available from: http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1317133826368
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GLOSSARY

2, 3, 4 G	2nd to 4th Generation Mobile Communication Systems
ACTH	Adrenocorticotropic Hormone
AEP	Auditory Evoked Potential
AGNIR	Independent Advisory Group on Non-Ionizing Radiation
AIF	Apoptosis Inducing Factor
AM	Amplitude Modulation
AMPS	Advanced Mobile Phone System (analog)
ANOVA	Analysis of Variance
CAS	Contralateral Acoustic Stimulation
CASA	Computer Assisted Sperm Analysis
CAT	Catalase
CDMA	Code Division Multiple Access
CNS	Central Nervous System
CW	Continuous Radiofrequency Wave
DAB	Digital Audio Broadcasting
DBMA	Dimethylbenz *(A)*anthracene
DCS	Digital-Coded Squelch
DECT	Digital Enhanced Cordless Telecommunications
DEN	Diethylnitrosamine
DMBA	7,12-Dimethylbenz(a)anthracene
DNA	Deoxyribonucleic acid
DPOEA	Distortion Product Otoacoustic Emission
EEG	Electroencephalography
EFHRAN	European Health Risk Assessment Network on Electromagnetic Fields
EHF	Extremely High Frequency
EHS	Electromagnetic Hypersensitivity Syndrome
EIRP	Equivalent Isotropically Radiated Power
ELF	Extremely Low Frequency
EMF	Electromagnetic Fields
ENU	N-ethyl-N-nitrosourea
EPRI	Electric Power Research Institute
FCC	Federal Communications Commission
FDG	Fluorodeoxyglucose
FDMA	Frequency Division Multiplexing Access
FOPH	Swiss Federal Office of Public Health

FM	Frequency Modulation
GHz	Gigahertz
GPx	Glutathione peroxidase
GSM	Global System for Mobile Communication
HAN	Home Area Network
HF	High Frequency
Hz	Hertz
hsp	heat shock protein
HSPA	High Speed Packet Access
HSDPA	High Speed Downlink Packet Access
ICNIRP	International Commission on Non-Ionizing Radiation Protection
IEEE	Institute of Electrical and Electronics Engineers
IEI	Idiopathic Environmental Intolerance
ISM Band	Industrial, Scientific, and Medical
Kg	Kilogram
LAN	Local Area Network
LF	Low Frequency
LTE	Long Term Evolution
MANOVA	Multivariate Analysis of Variance
MBPS	Mobile Phone Base Station
MCS	Multiple Chemical Sensitivities
MDA	Malondialdehyde
MF	Medium Frequency
MRI	Magnetic Resonance Imaging
MHz	Megahertz
MPBS	Mobile Phone Base Station
MX	3-Chlor-4-(dichloromethy)-5-Hudroxy-2-(5h)furanone
NIRS	Near Infrared Spectroscopy
NMR	Nuclear Magnetic Resonance
NSPS	Non-Specific Physical Symptoms
ODC	Ornithine Decarboxylase
OER	Observed Expected Ratios
OFDMA	Orthogonal Frequency Division Multiple Access
OR	Odds Ratio
PKC	Protein Kinase C
PEM	Personal Exposure Meters
PET	Positive Emission Tomography

PMA	Phorbol-12-myrystate-13 acetate
PTA	Pure Tone Audiometry
PW	Pulse Wave
PWC	Power Control
PTA	Pure Tone Audiometry
rCBF	Regional Cerebral Blood Flow
RF	Radiofrequency
RFA	RF Ablation
RF-EMF	Radiofrequency Electromagnetic Fields
RMS	Root-Mean-Square
RNA	Ribonucleic Acid
ROS	Reactive Oxygen Species
RR	Relative Risk
SAR	Specific Absorption Rate
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SMP	Software Modified Phone
SMR	Standardized Mortality Ratio
SOD	Superoxide Dismutase
TAC	Total Antioxidant Capacity
TDMA	Time Division Multiple Access
TEM	Transverse Electromagnetic Cell
TEOAE	Transiently Evoked Otoacoustic Emissions
TETRA	Terrestial Trunked Radio
TPA	12-O-tetradecanoylphorbol-13-acetate
UHF	Ultra High Frequency
ULF	Ultra Low Frequency
UMTS	Universal Mobile Telecommunications Systems
USB	Universal Serial Bus
VGCC	Voltage-Gated Calcium Channels
VHF	Very High Frequency
VLF	Very Low Frequency
W	Watts
WCDMA	Wideband CDMA (Code Division Multiple Access)
WHO	World Health Organization
WiFi	Wireless Fidelity, Wireless Internet
WiMax	Worldwide Interoperability for Microwave Access
WLAN	Wireless Local Area Networks