# INTEROCC: Occupational exposure assessment for electromagnetic fields and risk of brain tumours

## Development of a new source-based approach

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DOCTORAL THESIS UPF / 2016

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*“All events, even those which by their smallness and their irregularity seem to not depend upon the general system of nature, are a series as necessary as the revolutions of the Sun… The word chance expresses thus only our ignorance of the causes of the phenomena which we see to happen and to succeed themselves without any apparent order.”*

P.S. Laplace

Theory of chances (1783)

To my family, in particular to my dad and my wife, Sarah, for their endless support and their helpful advice.

# Acknowledgements

I would like to sincerely thank my supervisor, Prof Elisabeth Cardis, for the opportunity to join her Radiation team at CREAL, for her guidance, and especially for sharing her invaluable expertise and wisdom. Dr Joseph (Joe) Bowman has similarly been a guiding light throughout the PhD process, regularly putting me on the right track with his years of valuable experience at university and in the field. Jordi Figuerola, has been an irreplaceable technical support and I certainly could not have completed this work without his help. Laurel Kincl and Lesley Richardson for being so welcoming during my time at Oregon State University and Université de Montréal respectively, you made my time abroad really worthwhile and I am very grateful for the chance we had to work together. Michelle Turner, for always being ready to listen and provide valuable advice. Dave Conover, who I didn't have the pleasure to meet in person, but whose work provide an essential platform for the completion of the RF section. Ester Gracia and Ana Espinosa, have been tremendously helpful in the final stages of this work helping to solve my never ending doubts in statistics! I would like to thank Manolis Kogevinas, for his faith in me as an early stage researcher in CREAL. Finally, to my colleagues and friends at CREAL who have cheered me up in low moments and provided interesting discussions and beers! Mil gracias Alejandro Caceres, Ivan Dueñas, David Rojas, Cynthia Manzano, Nadja Espejo, Magda Bosch, and of course the various members of Sala C over the past four years – especially Laura Argenté and Montse Plazas for always being helpful and kind.

# Abstract

Introduction: Limitations in exposure assessment, for electromagnetic fields (EMF) or other physical and chemical agents, is possibly the most frequent weakness highlighted in epidemiological studies. This thesis aimed to improve methodologies for exposure assessment of EMF in occupational settings developing a new method based on sources of exposure rather than job titles. It also aimed to make use of the methodologies developed to assess the possible association between occupational exposure to radiofrequency (RF) and intermediate frequency (IF) EMF and risk of glioma and meningioma – the two most prevalent types of primary brain tumours – using the large dataset of subjects in the INTEROCC study. Methods: An extensive literature review, based on the EMF sources identified by experts and the workers through responses to a detailed source-based questionnaire, was used to locate exposure measurements for the sources identified. The measurements selected, after the assessment of their quality and relevance for our study by EMF experts, were included into an occupational exposure measurement database (OEMD). These data, together with the experts' ratings previously obtained, were summarized into a source-exposure matrix (SEM), containing confidence-weighted mean estimates of exposure for all the sources in the OEMD by frequency band and dosimetry type. Mean estimates of exposure from the SEM were used to obtain individual indices of EMF cumulative exposure, making use of specific algorithms developed and the information collected from the subjects on determinants of exposure. Finally, cumulative exposure estimates for RF and IF EMF were used to assess occupational exposure and risk of brain tumours (glioma and meningioma) in the study population. Results: A total of 95 articles and technical reports were collected from the literature with measurements which were judged useful. The SEM was constructed containing confidence-weighted mean estimates of exposure for 312 EMF sources of exposure, covering the entire EMF frequency range (0 Hz-300 GHz). Overall there was no association between glioma or meningioma risk and the cumulative exposure estimates developed for RF EMF. However, some positive associations were identified in the highest exposed groups in the 1- to 4-year exposure window for glioma and in all windows for meningioma. A positive linear association was also found for both tumour types using exposure as a continuous variable. For IF EMF, some weak positive associations were also seen in the highest exposure groups in the exposure windows closest to the diagnosis/reference date, only for glioma. Conclusion: The methodologies developed represent a novel approach which may reduce exposure misclassification due to Berkson error and can also be useful to assess and summarize exposure data similar to that obtained in our study. The risk estimates obtained for glioma and recent RF and IF EMF exposures might reflect a possible role of high frequency EMF in the later stages of carcinogenesis (promotion and progression). However, the lack of association overall and the small number of subjects available for some of the analyses weaken the strengths of our results. Further studies are warranted, both using and improving our methods.

# Resum

Introducció: La limitació en l'avaluació de l'exposició tant als camps electromagnètics (CEM) com a altres agents físics o químics, és possiblement la debilitat més freqüentment apuntada en els estudis epidemiològics. Aquesta tesi té com a objectiu millorar la metodologia en l'avaluació de l'exposició dels CEM en els llocs de treball desenvolupant un nou mètode basat en les fonts d'exposició i no en els llocs de treball. També té com a objectiu fer ús de les metodologies desenvolupades per avaluar la possible associació entre l'exposició ocupacional a CEM de radiofreqüència (RF) i de freqüència intermèdia (FI) i el risc de glioma i meningioma - els dos tumors cerebrals primaris més freqüents – aplicades a l'estudi INTEROCC. Mètodes: A partir de les fonts de CEM identificades pels experts i els treballadors a través de les respostes obtingudes a un detallat qüestionari orientat a fonts, es realitza una extensa revisió de la literatura per identificar les mesures d'exposició de les fonts identificades. Les mesures seleccionades, després de que els experts en CEM n’avaluessin la seva qualitat i rellevància pel nostre estudi, es van incloure en una base de dades de mesures d'exposició ocupacional (OEMD). Aquestes dades, junt amb les qualificacions dels experts que es van obtenir prèviament, es van resumir en una matriu de fonts d’exposició (SEM), que conté estimacions de la mitjana ponderada per les qualificacions dels experts per a totes les fonts de la OEMD per banda de freqüència i tipus de dosimetria. Per obtenir les exposicions individuals acumulades a EMF es van utilitzar les estimacions de la mitjana de l’exposició de la SEM, fent ús d'algoritmes específicament desenvolupats i la informació recollida al qüestionari sobre els determinants de l'exposició. Finalment, l'exposició acumulada estimada a RF i FI CEM es va utilitzar per avaluar l'exposició ocupacional i el risc de tumors cerebrals (gliomes i meningiomes) en la població d'estudi. Resultats: Es van obtenir un total de 95 articles i informes tècnics de la literatura amb les mesures que es van considerar útils. La SEM es va construir amb les estimacions de la mitjana ponderada per la confiança de l'exposició de 312 fonts de CEM, que cobreixen tota la gamma de freqüències dels camps electromagnètics (0 Hz a 300 GHz). En general, no hi va haver associació entre el risc de glioma o meningioma i les estimacions d'exposició acumulada a CEM RF, tot i que es van observar associacions positives en els grups més exposats en la finestra d'exposició d'1 a 4 anys per glioma i en totes les finestres per meningioma. També es va trobar una associació lineal positiva pels dos tipus de tumors utilitzant l'exposició com a variable contínua. Per CEM FI, algunes associacions positives febles també es van observar en els grups més exposats en les finestres més properes a la data de diagnòstic / de referència, només per a glioma. Conclusió: Les metodologies desenvolupades representen un enfocament innovador que pot reduir l'error en la classificació de l’exposició a causa de l’error Berkson i també poden ser útils per avaluar i resumir dades d'exposició similars a les obtingudes en el nostre estudi. Les estimacions de risc obtingudes per glioma i CEM RF i FI poden reflectir un possible paper dels CEM’s d'alta freqüència en les últimes etapes de la carcinogènesi (promoció i progressió). No obstant això, la manca d'associació global i el petit nombre de subjectes en alguns dels anàlisis debiliten la fortalesa dels nostres resultats. Calen més estudis, tant utilitzant com millorant els nostres mètodes.

# Preface

In this thesis, I worked, together with multiple co-authors and colleagues, in the development of a novel approach for exposure assessment of electromagnetic fields (EMF) in the workplace, based on sources of exposure rather than the traditional method of using job titles or occupations. In creating this new approach, we also developed new methodologies for assessing and combining exposure data from the literature, which can be useful for other occupational and environmental agents with characteristics similar to the exposure data collected in our study, INTEROCC. These methods were used to assess brain tumours risk associated with occupational exposure to high frequency EMF, making use of the largest dataset of subjects to date with the required information available. Although the ideas to build this novel methodology were developed before I joined the INTEROCC team, I expect that the work done and the results explained in this document will prove my contribution to the project.

The thesis appears in the context of a new European Directive (Directive 2013/35/EU) for the control of worker´s exposure to EMF, which has been recently transposed into Spanish law (RD 299/2016). Although the methodologies and results obtained can be useful in any country, local occupational hygienists and experts involved in the assessment and control of EMF exposures at work in general will find them helpful.

This thesis has been written at the Centre for Research in Environmental Epidemiology, CREAL, now the Barcelona Institute for Global Health, ISGlobal (Barcelona, Spain) between 2012 and 2016 and supervised by Prof. Elisabeth Cardis. It consists of a compilation of scientific publications in agreement with the regulation of the Doctoral Programme in Biomedicine of the Department of Experimental and Health Sciences at the Pompeu Fabra University. This thesis includes an abstract, a general introduction, a thesis justification, the main aim and objectives, the methods and the results (a compilation of three research publications with commentary as well as a summary of a fourth publication which is under preparation), an overall discussion section and final conclusions and recommendations. Important concepts have been Italianised and can be located using the Alphabetical Index.

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## LIST OF ABBREVIATIONS

B-field: Magnetic flux density, in microTesla (μT) [low frequency fields]

DECT: Digital Enhanced Cordless Telecommunications

E-field: Electric field strength, in volts per meter (V/m)

ELF: Extremely Low Frequency (3-3000 Hz)

EMF: Electromagnetic fields

GHz: Giga Hertz

GSD: Geometric Standard Deviation

H-field: Magnetic field strength, in amperes per meter (A/m) [high frequency fields]

Hz: Hertz

IARC: International Agency for Research on Cancer

ICNIRP: International Commission on Non-Ionizing Radiation Protection

IF: Intermediate Frequency (3 kHz – 10 MHz)

kHz: Kilo Hertz

MHz: Mega Hertz

MRI: Magnetic Resonance Imaging

OEL: Occupational Exposure Limit

OEMD: Occupational Exposure Measurement Database

PD: Power Density, in watts per square meter (W/m2)

RF ID: Radio Frequency Identification

RF: Radiofrequency (10 MHz – 300 GHz)

RL: Reference Level

SAR: Specific Absorption Rate

SD: Standard Deviation

SEM: Source Exposure Matrix

SMF: Static Magnetic Fields, in microTesla (μT), 0 Hz

TLV: Threshold Limit Value

# 1. INTRODUCTION

## 1.1 Electromagnetic fields (EMF) basics

Radiation is the transmission of energy through space or matter in the form of waves or particles. The electromagnetic spectrum (Fig. 1) can be divided into ionizing and non-ionizing radiation, depending on the frequency (measured in Hertz, Hz, or cycles per second) and the amount of energy transported. Ionizing radiation (i.e. from high-energy ultraviolet radiation to gamma rays) comprises forms of radiation with sufficient energy to ionize, that is, to break atoms or molecules releasing some of their electrons. Non-ionizing radiations (NIR), on the contrary, do not have sufficient energy to ionize matter. These include several forms of electric and magnetic fields (EMF), with a range of frequencies from static fields (0 Hz) to frequencies near visible light (~300 GHz). EMF are field forces created by circulating charged particles which give rise to oscillating electric and magnetic fields. EMF are, therefore, characterized by their frequency as well as their intensity (the magnitude of the field). EMF are vector quantities, with magnitude and direction, and can be either static or propagate through the space (vacuum) in the form of waves (Hitchcock and Patterson, 1995; Hitchcock, RT, 2015).

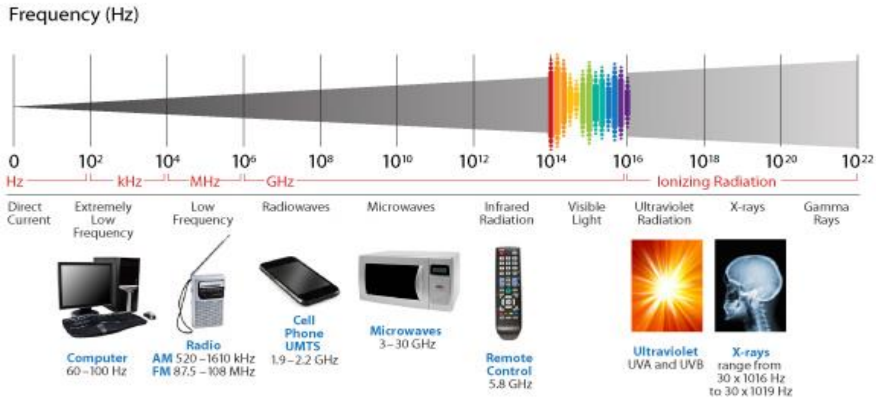

**Figure 1**: The electromagnetic spectrum. Source: www.niehs.nih.gov/ /health/topics/agents/emf/

Electromagnetic waves can be characterized by three related quantities, *wavelength*, frequency and intensity (energy). Wavelength, designated by the Greek letter lambda (λ), is the distance between any two points of a wave which define an entire cycle. By convention, wavelength is commonly used to describe electromagnetic energies such as ultraviolet, visible, and infrared radiation. Frequency is defined as the number of complete cycles per second. Its unit is the Hertz (Hz), in memory of the German physicist Heinrich R. Hertz, who discovered the propagation of EMF. Frequency is commonly used to describe the part of the EMF spectrum from static magnetic fields (0 Hz) to 300 GHz. Although several definitions exist, fields originating within the NIR range can be divided into three main bands of frequencies. For the purpose of the projects in which this thesis was conducted (INTEROCC/GERoNiMO), these bands were defined as follows: *Extremely Low Frequency* (ELF) fields (3-3000 Hz), *Intermediate Frequency* (IF) fields (3 kHz-10 MHz), and *Radiofrequency* (RF) fields (10 MHz-300 GHz). Microwaves are usually defined within the highest part of the RF range (i.e. 300 MHz – 300 GHz). *Static magnetic fields* (SMF) do not vary in time or space and, therefore, their frequency is 0 Hz.

Depending on the type of EMF, a variety of quantities and units are commonly used to describe them. *Electric field strength* (E-field) is measured in Volts per metre (V/m). Magnetic fields are characterised by two components, the *magnetic field strength* (H- field) and the *magnetic flux density* (B-field). H-fields are measured in Amperes per metre (A/m) whereas B fields are measured in Tesla (T) or Gauss (G), and, more commonly, in micro Tesla (µT) or mili Gauss (mG) [1 µT=10 mG]. H-fields are commonly used to describe high-frequency magnetic fields while B-field are used with lower frequencies. Traditionally, frequency bands have been defined for their use in telecommunication. Although other definitions for high frequency EMF exist (ICNIRP, 2009), for the purpose of this thesis high frequency refers here to frequencies above 3 kHz up to 300 GHz.

## 1.2 Sources of electric and magnetic fields

Many natural and man-made sources of electromagnetic fields exist. The most important natural source of RF radiation is the sun, while natural magnetic fields are created by static geomagnetic forces. Man-made EMF sources have increased the amount and frequency of the overall exposure to EMF that we all receive. For the purpose of this work, an EMF source was considered any device or equipment which emits electric, magnetic or electromagnetic fields either as part of its normal function or as a secondary effect of the use of electricity.

## 1.3 Radiofrequency electric and magnetic fields

Radiofrequency EMF are characterized by their high frequency and energy which gives them the capacity to heat matter. These fields propagate through space in the form of waves. The electric and magnetic components of the wave are orthogonal to each other and have a fixed ratio of intensity. Their intensity decreases inversely with the distance (r) at a rate from around 1/r to $1/r^2$, depending on the type of emitting source (Figure 2). Different sources may lead to RF EMF with different patterns of propagation. For instance, transmitters, broadcasting and mobile phone antennas may have a mixture of patterns which vary with the distance from the source. Sources of RF EMF may also emit in other frequencies, including static, ELF and/or IF (e.g. mobile phones and other transmitters can emit both RF and ELF EMF), although main emissions are produced within the RF range (Hitchcock and Patterson, 1995; Hitchcock, RT, 2015).

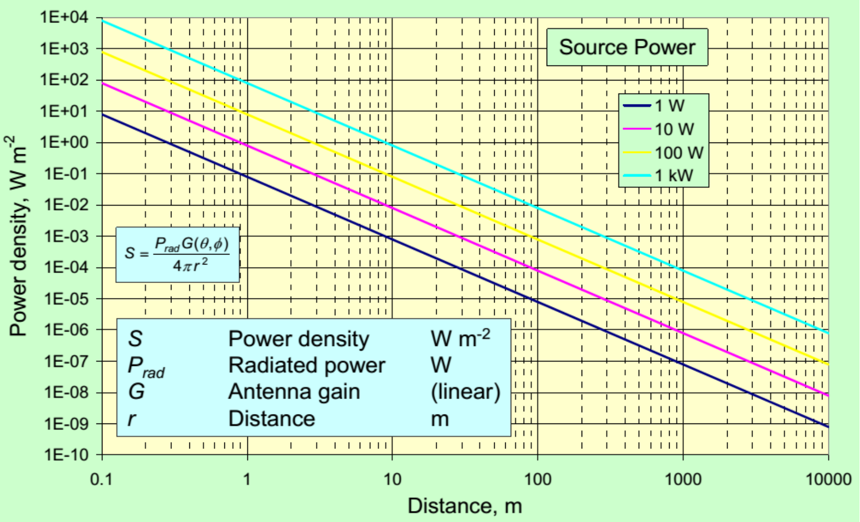

**Figure 2**. Power density versus distance for various antennas with different radiated powers in Watts (Mann, 2011).

The measurement of RF EMF uses several quantities including *power density* (PD or also called S, from Specific Power), *electric field strength* (E-field), and *magnetic field strength* (H-field). Power density is the power incident on a surface divided by its area. In the International System of units (SI), the unit is Watts per square meter (W/$m^2$). Although E- and H-fields are vector quantities – they have magnitude and direction –, they are generally treated as just magnitudes, since only these are usually measured and reported in safety evaluations. The relationship between these three quantities is explained by Ohm´s law. Thus, the PD of an electromagnetic field is directly proportional to the product of the electric and the magnetic fields:

$$PD(W/m^2) = E(V/m) * H(A/m) \tag{1}$$

Physical characteristics of RF EMF differ with distance to the emitting source. In the *near field* (commonly defined as the space between the source and up to one *wavelength*), the relationships between electric and magnetic fields are complex and they can be considered independent. In the *far field* (i.e. more than one *wavelength* from the source), however, the characteristics are more homogeneous and a clear relationship exists between these two quantities:

$$E[V/m] = H[A/m] * 377 ohms \tag{2}$$

where 377 ohms equals the *impedance* of free space.

Other quantities used to characterize RF EMF are *specific absorption* (SA) and *specific absorption rate* (SAR). These quantities describe the RF EMF dose and dose rate as they refer to the amount of energy absorbed by the body or any other matter. Other dose metrics commonly encountered in the EMF literature are *internal electric field* and *induced current density*. These quantities are more difficult to measure since they are produced inside the body, although mathematical models have been recently developed (Chen et al., 2013; Findlay, 2014) in an effort to estimate internal dose when direct measurements are not possible or feasible.

### 1.4 Extremely-low frequency electric and magnetic fields

Electric and magnetic fields at *extremely low frequencies* (ELF), are the fields in the lowest section of the *electromagnetic spectrum* (>0–3000 Hz), just above *static magnetic fields*. These are field forces exerted by electricity, hence a vast number and varieties of sources exist, depending on whether electricity is produced (e.g. power plants), distributed (e.g. power lines) or used (e.g. electric appliances, computers). Unlike RF EMF, ELF electric and magnetic fields are unsynchronized fields as they are *near fields*. Their possible effects on the body depend on their frequency, through *magnetic induction* (Bowman JD, 2014). ELF EMF sources may also emit fields in other frequencies, especially *static magnetic fields* and IF EMF. As RF EMF, the magnitude of ELF EMF also decreases with distance, and this decline is somewhat faster, with a range between $1/r^2$ and $1/r^3$ (1,2) (Figure 3).

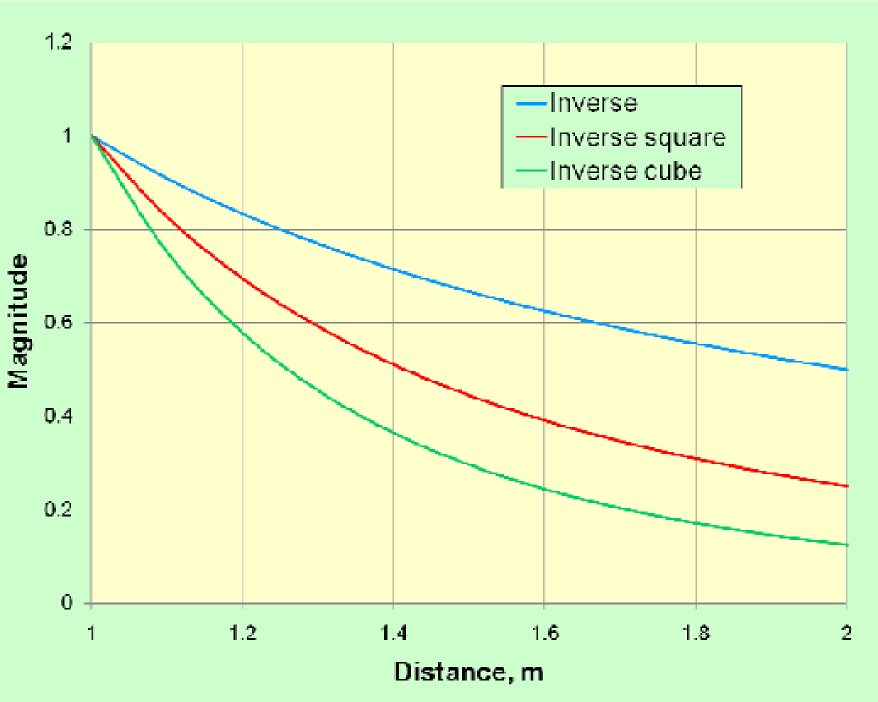

**Figure 3**. Magnetic fields versus distance for various ELF MF sources. The decrease rate of the MF magnitude varies depending on the source characteristics (Mann, 2011).

## 1.5 Intermediate frequency electric and magnetic fields

EMF in the *intermediate frequency* (IF) range (3 kHz – 10 MHz) have been recently considered as a new entity. Although they share characteristics with ELF and RF EMF, they have been commonly considered within the low part of the RF range and very few studies exist until now which focused exclusively on this frequency range.

## 1.6 Interaction with matter

From a biological effect point of view, electric (E) and magnetic (B and H) fields are different physical agents and their effects on the body are conditioned by the frequency and magnitude (intensity) of the field. Fields with different frequencies interact with matter through different *biophysical mechanisms* which ultimately determine their biological effects. The potential for biologic effects is associated with power deposition and the *squared field strengths* are proportional to *power* (Hitchcock and Patterson, 1995; Hitchcock 2015). Frequency is key to understand the potentials for health damage from EMF, since it determines the type of molecular mechanisms which may occur within the body (e.g. electrostimulation, heating, biochemical impairment). RF EMF have enough energy to cause temperature rise within the body, which has been traditionally used as a measure of internal dose. ELF magnetic fields can give rise to internal electric fields in the body which depend on the magnitude and the frequency of the ELF MF. Little is known regarding the biophysical effects of IF electric and magnetic fields. However, since they share many characteristics with RF and ELF, their internal effects can go from *electrostimulation* and *induced electric fields* to *heating*, depend on the actual frequency.

All matter interacts with electric fields, which usually causes a decrease of intensity. Magnetic fields, on the contrary, are not so easily disturbed, except by ferromagnetic metals (e.g. iron, nickel). The interaction with these metals can cause either increase or decrease of intensity, depending on the geometry (Bowman JD, 2014).

## 1.7 Occupational exposure to EMF

Occupational exposure to EMF occurs wherever electricity is generated, distributed or used, as well as when EMF emitting technologies are used in the workplace. Numerous technologies used in occupational settings are responsible for EMF emissions and the number and diversity of EMF sources have increased enormously in the last century. Static magnetic fields exposure affects mainly health workers through the use of MRIs and similar technologies, as well as drivers of trains and other electric equipment. Exposure to ELF fields occurs in electric utility workers and others who use or work near electric appliances (e.g. computers, sewing machines and ovens). IF fields are mostly related to the use of new applications (e.g. *induction heating,* and *anti-theft gates*) while exposure to RF fields is mostly associated with the use, maintenance and repair of telecommunication devices (e.g. radios, and radars) as well as some manufacturing and medical equipment (e.g. *welding, dielectric heating,* and *diathermy*).

For this thesis, information was collected for EMF sources in all frequencies (i.e. from SMF to RF). However, because a special emphasis was finally given to RF and IF exposures and sources, as well as for reasons of space, the following sections will mainly focus on these two frequencies.

### 1.7.1 Occupational sources of RF EMF exposure

Within the INTEROCC project, sources of *radiofrequency* EMF were classified in 7 main occupational sections or sectors: 1. Diagnosis and treatment; 2 & 3. industrial and food/medical heating; 4. Semiconductors; 5. Radars; 6 & 7. Telecommunication antennas and transmitters. Among the different frequencies used by the RF EMF sources in these sectors, 13.56 and 27.12 MHz are the most common frequencies, since international organizations, such as the Federal Communications Commission (FCC) and the International Telecommunications Union (ITU), have traditionally allowed the use of these frequencies for industrial, scientific or medical applications.

#### 1.7.1.1 RF-EMF sources used for diagnosis & treatment

Several types of equipment used in the diagnosis and treatment of disease lead to RF-EMF exposures. *Diathermy* units are used in *physical therapy*. Heat is commonly applied to patients to achieve muscle relaxation or other purposes. The most common technologies used are *ultrasonic*, *shortwave* (13.56 or 27.12 MHz) and *microwave* (915 MHz or 2.45 GHz). Overexposure of applicator may occur in the vicinity of the cables, while the physiotherapist adjusts the equipment during operation. Electric and magnetic exposure levels can reach up to 2,000 V/m and 3 A/m, respectably. *Electrosurgical devices* are used to cauterize or coagulate tissues. Common frequencies are between 0.5 and 2.4 MHz. Exposure levels can reach up to 500 V/m near an active equipment (Floderus et al., 2002; Hitchcock, RT, 2015; Liljestrand et al., 2003; Mantiply et al., 1997).

#### 1.7.1.2 RF-EMF sources used for industrial heating

*Dielectric heaters*, also called RF sealers/welders, are used to heat dielectric materials, mainly plastics, fabrics, wood and paper. These devices can weld, mould or seal plastics or cure glues and resins. The most common frequency of operation is 27 MHz, although lower frequencies such as 13.56 MHz are also common. Some devices can reach frequencies up to 70 MHz (Hitchcock, RT, 2015). Other frequencies are also in use and some plastic sealers can work with frequency ranges between 6.5 and 65 MHz. High exposure levels, especially to E-fields, have been identified in multiple workplace evaluations (Allen et al., 1994; Bini et al., 1986; Conover et al., 1992; Stuchly et al., 1980; Wilén et al., 2004). *RF heaters* (Figure 4) are considered the most common source of excessive emissions of RF fields (ICNIRP, 1998a), with average E-field levels around 400 V/m and maximum values above 2,000 V/m (Hitchcock and Patterson, 1995).

**Figure 4**. Radiofrequency (dielectric) heater. Adapted from Google® images.

RF plastic sealers can be classified depending on the material being heated and their general appearance. *Sealing machines, shuttle trays, turntables* and *pressure sealed applicators* are the most common subtypes used for heating plastics (Stuchly et al., 1980). *Edge glue* *dryers* are used to heat, cure and/or dry glue, which is then used for joining wood pieces. Typical frequencies used range from 4 to 50 MHz (Joyner and Bangay, 1986; Stuchly et al., 1980).

#### 1.7.1.3 RF-EMF sources used in food heating

RF EMF sources are used to heat, cook, cure or sterilize foodstuff. Perhaps one of the most well-known device, since they are also common in most homes nowadays, are microwave ovens. Domestic ovens use frequencies of 2.45 GHz, while microwave ovens used in industrial and commercial premises often also use 915 MHz (Elder et al., 1974). Radiofrequency radiation is also used to sterilize food and other materials (e.g. soils, wastewater).

#### 1.7.1.4 RF-EMF sources in the semiconductors industry

In the chips processing industry, various types of plasma equipment are used with frequencies of 13.56 or 27.12 MHz (e.g. *plasma strippers*, *dry plasma etchers*, *plasma-enhanced chemical vapour deposition* (CVD) and *sputtering* or *metal deposition* equipment). Some workplace evaluations have demonstrated that RF leakage can occur even from well-maintained units. Emission levels for E-field range between 2-80 V/m (Cooper, 2002; Ungers et al., 1984).

#### 1.7.1.5 Radars

Most radars work in the microwave range of the RF band (i.e. 300 MHz – 300 GHz), using *pulse-modulated* modes and high transmitting powers (Hitchcock, RT, 2015). Overexposures may occur while performing maintenance tasks in the proximity of commercial radars (e.g. *airport traffic control*, *weather and airport surveillance*). Relatively high exposures are also possible inside *aircraft cockpits* (Tell et al., 1976; Tell and Nelson, 1974), near *marine radars* (Peak, 1975), and police speed devices (Bitran et al., 1992; Bradley, 1991; Fisher, 1993; Lotz et al., 1995). Little information exists in the literature about military radars (Figure 5), but some available measurements and modelling have shown exposure levels between 100-500 V/m at around 200 m of distance (Degrave et al., 2009; Szmigielski, 1996).

**Figure 5**. HAWK Low Power Illuminator military radar: frequency 10.25 GHz. Adapted from (Murata, Taichi K, 2015).

#### 1.7.1.6 Telecommunication antennas

Communication equipment may be fixed to buildings or built on the ground (e.g. *broadcasting antennas*). Fixed antennas are used for high frequency *radio*, *television*, *mobile phone*, *satellite* and *microwave* radio systems, among others. Overexposures may occur to maintenance workers while climbing or working on energized antennas on towers or buildings, or on the ground. Exposure levels vary depending on the specific source. E-field exposure of an operator working on a *mobile phone mast* can be around 13 V/m (Cleveland et al., 1995; Cooper et al., 2004), while *marine radio antennas* can lead to exposures over 100 V/m (Baste et al., 2010; Skotte, 1984; Tynes et al., 1996).

#### 1.7.1.7 Transmitters

Transmitters are typically mobile or portable communication devices, either handheld or attached to vehicles. They are frequently used by police, fire and other emergency services, but also by maintenance staff, security agencies and other industrial and commercial activities. Portable systems include *walkie talkies*, *cordless telephones*, *cellular phones* and *marine* and *airplane communication systems*. Transmitters commonly attached to vehicles include *citizen band* (CB) radio and other types of *two-way radios*. Analogical *cordless telephones* worked with frequencies around 50 MHz, while *cellular/mobile phones* and modern *DECT phones* work in the range between 450 up to 2200 MHz. Exposure levels depend on the power of the device and its frequency. *Electric field strengths* between 20-700 V/m have been measured near transmitters attached to vehicles working at 800 MHz. Hand-held transmitters or transceivers´ emissions occur near the head of the users, so recommended exposure limits can sometimes be exceeded (Hitchcock and Patterson, 1995; Lambdin and EPA, 1979; Ruggera, 1979).

### 1.7.2 Occupational sources of IF EMF exposure

Some RF sources can also emit in the IF range. AM and some FM radio antennas use frequencies between a few kHz up to 2 MHz. *Electric field strength* levels of workers in the vicinity of these antennas can be of up to 200 V/m. *Marine and naval radio antennas* use frequencies between 2.1 - 8 MHz, although typical E-field exposures tend to be slightly lower (Baste et al., 2010; Skotte, 1984; Tynes et al., 1996).

Recent years have seen an increase in the number and types of IF EMF emitting sources. *Induction heaters* are used in the industry to heat metals and other materials. Although some devices work with frequencies within the ELF and even the RF range, common frequencies are between 400 kHz and 2.4 GHz. Other induction technologies include *soldering* and *welding*. *Induction plates* are common in industrial and commercial premises, as well as in domestic settings. Some newer technologies include *security tags* and antennas (e.g. *electronic article surveillance*, EAS, and RF IDs). EAS devices (Figure 6) use frequencies between 58 kHz and 9.1 MHz and H-field exposures near them can reach around 25 A/m (Joseph et al., 2012a). RF IDs usually work in the range of 13.56 MHz.

**Figure 6**. Electronic article surveillance (EAS) antennas. Adapted from Google® images.

Some industrial devices in the IF range are less common such as high frequency food disinfection equipment (Figure 7), which have frequencies between 300 kHz to 10 MHz, and *high frequency welding* units used in the production of pipes, tubes and beams for spot welding of metal surfaces. HF welders usually operate at 400 to 450 kHz, although operational frequencies can reach 3 MHz. Like with other types of welding equipment, operators can get overexposed in the proximity of the cables, and especially when they encircle an arm or the abdomen with the cable because of the requirements of the specific task being performed. Power densities near the worker are around 10 W/m$^2$ (Hitchcock and Patterson, 1995; Repacholi, 1981).

**Figure 7**. Intermediate frequency heating equipment for food disinfection. (Lagunas-Solar et al., 2006)

### 1.7.3 Occupational sources of SMF and ELF EMF

Occupational sources of static magnetic fields (SMF) include MRIs (*magnetic resonance imaging* systems), *welding* and transportation systems (e.g. *train*, *metro*). SMF (0 Hz) emitted by these types of equipment can lead to very high magnetic field exposures. Repair technicians may experience B-field mean levels over 70 T (70 million µT). All electrical and electronic equipment emit ELF EMF to some extent. Electric and magnetic fields at *extremely low frequencies* are therefore emitted whenever electricity is generated, distributed or used. From *power lines* to *office appliances*, workers using or in the proximity of the devices may experience relatively high exposures which depend on the power of the device, its actual frequency and the distance to the source.

Given the scope of this thesis, SMF and ELF EMF sources are not explained here in detail. Further information on the sources which emit in these frequencies can be found elsewhere in the EMF literature (Bowman JD, 2014; Hitchcock and Patterson, 1995).

## 1.8 EMF exposure assessment

Exposure assessment for electric and magnetic fields goes back at least to 1979, when Wertheimer and Leeper assessed the risk of childhood leukaemia using the electrical configurations of the children´s homes as a surrogate of ELF EMF exposures (Wertheimer and Leeper, 1979). Since then, exposure assessment methods have improved notably. In the 1980´s, grouping of job tiles, such as "*electrical occupations*", were used as a potentially higher exposed subpopulation of workers (Loomis and Savitz, 1990). Subjects were assigned to groups of electrical and non-electrical jobs or were grouped into exposure categories (e.g. possible, probable and no exposure). With the improvement and increased availability of measurement devices for EMF since the mid 80´s, these qualitative assessments gave way to an ever increasing number of quantitative assessments. Personal meters for ELF MF developed rapidly, given the increase interest to study leukaemia in children after the famous 1979´s study. Among them, perhaps the most well-known are the EMDEX® family, still in much use nowadays. Personal exposure meters for radiofrequency EMF have improved their quality and accuracy as well as their portability in recent times (Figure 8) (Mann, 2010; Mann S et al., 2005). Meters for IF EMF are still rare but studies using new technologies are increasingly frequent (Joseph et al., 2012b; Van Den Bossche et al., 2015).

**Figure 8.** Radiofrequency E-field personal exposure meter. (Mann, 2010).

The net exposure to electric and magnetic fields of a person is created by the sum of the fields in his/her proximity, including the *static magnetic fields* emitted by the earth or any other natural sources. Because EMF vary in space and time, to summarize a person´s exposure into an instantaneous single number, an exposure metric must combine the frequency and the spatial and temporal characteristics of the field (Bowman JD, Kelsh MA, Kaune WT, 1998). Some common metrics are the *root mean square* (RMS) and *peak vector magnitudes*. These metrics can be measured with a wide range of instruments which have been specifically designed to measure fields in different frequency bands (SMF, ELF, IF or RF). The intensity of the electromagnetic field varies with the distance from the source and hence personal measurements must consider location and position of the body in relation to the emitting EMF source. For studies of long-term effects, the time-weighted average (TWA) has been the most commonly used metric to summarize the net ELF-EMF exposure of a person, as it allows the assessment of cumulative exposure (Bowman JD, 2014). Other summary statistics, such as the arithmetic and the geometric means, are also commonly used. EMF data – like many other environmental and occupational agents – tend to be log-normally distributed, that is, the data are strongly skewed to the right (long tail), with many low intensity and a few high intensity values. Therefore, the geometric mean is the statistic that best represents the middle value in that type of distributions. However, if the interest in the middle value focuses more on cumulative exposure, or dose, than on typical exposure levels at a moment in time and space, the arithmetic mean is a more appropriate measure of central tendency (Pfetzing E, Allen B, 1994).

Measurement of EMF at work may be performed with portable dosimeters, whereby EMF can be monitored throughout a few hours or an entire work shift. These type of measurements are the most representative of *personal* exposure but can be expensive and time-consuming. Other measurements can be obtained by placing the meter at a specific distance from the EMF-emitting source, either at a location typically used by the worker (i.e. *operator position* measurement) or at various distances from the source (*spot* measurement).

## 1.9 Industrial Hygiene for EMF

Guidelines for occupational exposure to EMF have been proposed by several international organizations, including the International

Commission on Non Ionizing Radiation Protection (ICNIRP), the American Conference of Governmental Industrial Hygienists (ACGIH), the Institute of Electrical and Electronics Engineers (IEEE), or the National Council on Radiation Protection and Measurements (NCRP). These institutions have commonly issued exposure limits for both the general public and for workers. *Occupational exposure limits*, and *reference levels*, can be of the same magnitude as those for the general public or higher. The limits established by the ACGIH are called *threshold limit values* (TLVs). TLVs have been established for all frequencies and are regularly updated in order to adapt them to the increasing EMF and health evidence. Exposure limits are derived from *basic restrictions* by mathematical modelling and extrapolation of laboratory findings. Basic restrictions are dosimetric quantities obtained in the laboratory in reference to various well-known acute effects (i.e. mainly electrostimulation for low frequency fields and heating for high frequencies). For RF, they include *internal or "in situ" electric field strength*, *specific energy absorption* (SA), *specific energy absorption rate* (SAR) and *power density* (PD or S), which is both a basic restriction and a derived reference level. SAR and PD are basic restrictions for the portion of the RF spectrum which can produce adverse tissue heating (100 kHz – 300 GHz). SAR applies to the lower part of this range, which may differ depending on the guidelines (e.g. 100 kHz – 3 GHz for ACGIH, and 100 kHz – 10 GHz for ICNIRP). PD applies to the upper part of the RF range (Hitchcock, RT, 2015; ICNIRP, 1998a). For low frequency fields, basic restrictions are provided as *current density* (in mA/m$^2$) to limit the effects on the nervous system function. In the 100 kHz – 10 MHz range, basic restrictions are provided as both SAR and *current density,* since both nervous system stimulation and heating may occur. Reference levels are intended as averaged levels over the entire body of the exposed individual, with the constraint that basic restrictions are not exceeded. Reference levels are established in the common magnitudes and units used for incident electric and magnetic fields and vary depending on the frequency. Figure 9 shows the reference levels established by ICNIRP for exposure to time varying electric fields, including occupational and residential average and peak values.

Based on the levels established by ICNIRP and other international bodies, several countries and regions, such as the European Union, have adopted their own limits. A new EU directive (Directive 2013/35/EU) was approved in 2013, containing the minimum health and safety requirements for workers in relation to exposure to EMF. Spain, like other European countries, has recently adopted this directive by transposing this directive into its own national regulation. One of the main aspects of the directive, and the transpositions adopted by the member states, is the need for assessing the risk posed to workers from exposure to EMF sources. Among other things, this assessment involves the compliance of specific exposure *reference levels* by frequency, to ensure that *occupational exposure limits* (OELs) are not breached (European Parliament and Council, 2013).

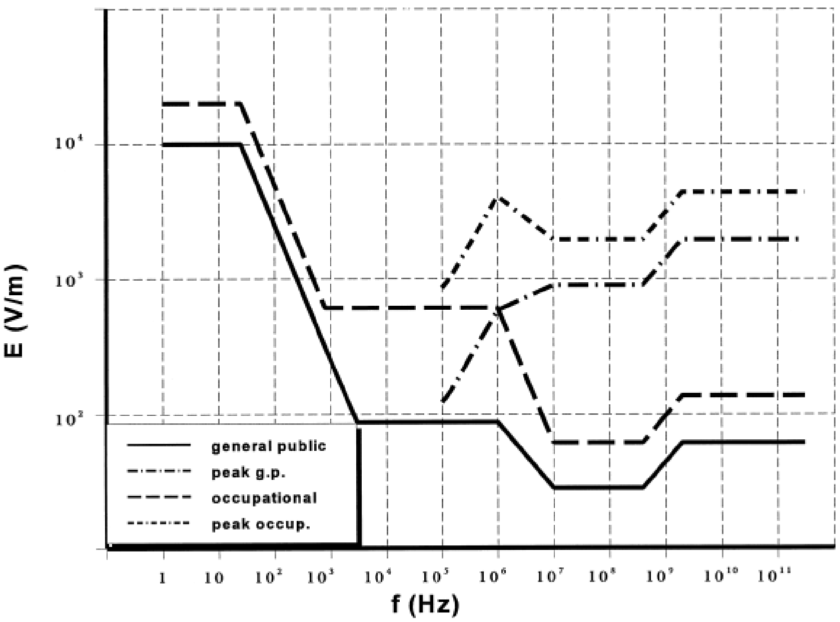

**Figure 9**. Reference levels for time-varying electric fields. (ICNIRP, 1998b).

## 1.10 Exposure to EMF and Health

Although there is evidence that exposures to high intensities of EMF may cause acute neurological and other health-ill effects (Röösli M, 2014), the majority of research on EMF and health has focused on chronic effects. The existing epidemiologic evidence suggests that exposure to both ELF and RF EMF may increase the risk of brain and other cancer types (Baan et al., 2011; Coble et al., 2009; Sienkiewicz Z, Schüz J, Poulsen AH, Cardis E, 2012). As a result, in 2011, the International Agency for Research on Cancer (IARC) Monograph Working Group classified RF (electric fields) as “possibly carcinogenic to humans” (Group 2B), based on limited evidence in humans from studies of brain tumours in relation to wireless telephone use and in experimental animals. In 2002, ELF MF had also been classified as Group 2B by IARC, based on limited evidence in humans from studies of residential exposure and childhood leukaemia (IARC, 2013, 2002). However, the evidence for brain and other tumours in relation to occupational RF and ELF exposure was judged inadequate.

## 1.11 Epidemiology of EMF and brain cancer

Although some studies indicate a gradual increased incidence of brain cancer over all, the incidence for some subtypes such as glioma and meningioma - the most common types of primary brain tumours - , has been fairly stable over the past 30 years (Ostrom et al., 2014). An important explanation for at least part of the possible apparent increase in incidence for all brain cancers is the improvements in diagnostic technologies and the ability to identify more cases (Bondy et al., 2008). A larger incidence in males, however, has been clearly seen in many countries, suggesting a possible association with occupational risk factors (Karipidis et al., 2007).

Ionizing radiation is one of the few risk factors widely accepted as a cause for brain cancer (Bondy et al., 2008; Ostrom et al., 2014). The association of this serious disease with non-ionizing radiation, particularly with RF and ELF EMF, has been extensively studied (Speers et al., 1988; Juutilainen et al., 1990; Tynes et al., 1994; Kheifets et al., 1995; Cardis et al., 2007; Hardell et al., 2013; Sadetzki et al., 2014). However, the evidence is still weak and the problem remains unresolved (Bondy et al., 2008). Since primary brain tumours are a rare disease, the most frequent design has been the case-control study. These type of studies commonly suffer from several limitations, especially the need to assess exposures retrospectively, since obtaining measurements from the past is frequently not possible. Studies based solely on subjects' questionnaires may suffer from recall bias, particularly among cases, given the cognitive impairment in some of the subjects in more advanced phases of the disease. Overall, results have been inconsistent, with many reduced risks and some non-significant positive associations, commonly in the highest exposed groups studied. The studies on brain tumours and exposure to RF EMF from mobile phones (Cardis et al., 2007; Interphone Study Group 2010, Cardis et al 2012, Hardell et al., 2013; Sadetzki et al., 2014; Coureau et al., 2014) have been of special relevance, given the widespread use of these devices for telecommunication and other purposes. Most of them relied on questionnaires and only recently exposure measurements and modelling efforts are being carried out. Some cohort studies have been performed or are being undertaken for both RF EMF (Schüz et al., 2011) and ELF EMF (Koeman et al., 2014). These also tend to rely on questionnaires or operator records and few or none actual exposure measurements are used.

The association between occupational exposure to EMF and brain cancer risk has also been broadly studied. Typically, studies looked at exposures of workers commonly associated with high exposures to either ELF EMF (Loomis and Savitz, 1990; Floderus et al., 1993; Savitz and Loomis, 1995; Harrington et al., 1997; Rodvall et al., 1998; Savitz et al., 2000; Sorahan et al., 2001; Navas-Acién et al., 2002; Villeneuve et al., 2002; Håkansson et al., 2002; Karipidis et al., 2007; Coble et al., 2009; Schüz et al., 2011; Koeman et al., 2014;

Turner et al., 2014) or RF EMF (Lilienfeld, 1978; Robinette et al., 1980; Milham, 1988; Tynes et al., 1994; Szmigielski, 1996; Lagorio et al., 1997; Finkelstein, 1998; Morgan et al., 2000; Groves et al., 2002), although some studies looked at the effects from both frequencies (Karipidis et al., 2007b). Results from meta-analyses for ELF EMF and brain cancer (Kheifets et al., 1995; Kheifets, 2001; Kheifets et al., 2008) showed small increases in risk estimates of around 10-20%. However, the lack of a clear pattern over all studies reduces our capacity to support this hypothesis. For RF EMF, studies have been mostly negative although some positive associations were identified among *radio* and *telegraph operators* (Tynes et al., 1994), *plastic-ware workers* (Lagorio et al., 1997) and *military personnel* (Szmigielski, 1996), but they were mostly non-significant. Most of these studies included few exposed subjects and had limited exposure assessment, mainly based on job titles or type of work. Negative studies were usually based on questionnaires and various exposures surrogates while studies which found positive associations frequently used actual measurements of RF EMF.

### 1.12 Biophysical effects and mechanisms

Because human data are still limited, scientists have relied on animal and cell models to establish biological effects from exposure to EMF as well as hypotheses about the potential mechanisms behind. For RF, acute or short-term effects due to overexposures have been observed in behavioural studies, including *reversible disruption* and other neurological symptoms (e.g. headache, irritability). These effects seem to be driven by increases of body temperature via the absorption of RF energy. Reproductive and developmental effects as well as ocular effects have also been reported in the laboratory, although these studies have not demonstrated any trends (Hitchcock, RT, 2015). Neurological acute effects from exposure el ELF EMF have also been reported, including *sleep disorders*, *tinnitus* and *dizziness*, while the existence of a true *electromagnetic hypersensitivity syndrome* is still under discussion (Mueller et al., 2002). Regarding chronic effects, some in vivo data from animal studies suggest that microwaves may be a tumour promoter, while others have demonstrated no significant differences between exposed and non-exposed groups.

Several mechanisms (e.g. *melatonin repression*, *oxidative stress*, *calcium channels impairment*) have been proposed although, until now, none of them are fully accepted by the entire scientific community. Although, overall, the laboratory data can be considered inconclusive, new studies are shedding more light into the possible effects and mechanisms involved. For instance, a new study performed by the US National Toxicology Program (NTP) reported a significant increase in tumours among male rats exposed to RF EMF (Wyde et al., 2016). In addition, it has been announced that NTP results on DNA damage will be released soon (http://microwavenews.com/news-center/ntp-comet-assay).

# 2. THESIS JUSTIFICATION

Until now, the ability of epidemiological studies to draw clear inferences between EMF exposures and health outcomes such as cancer has been reduced by limitations in exposure assessment and small sample sizes available. Moreover, the assessment of occupational exposures to EMF has been mainly limited to the assessment of ELF fields, using existing or newly developed ELF-MF job-exposure matrices (JEMs) (Bowman et al., 2007; Burau et al., 1998; Forssén et al., 2004; Gobba et al., 2011), direct measurements, or semi-quantitative and qualitative methods. However, the high between-worker variability associated with EMF exposures, as well as with other occupational agents (Kromhout et al., 1993; Rappaport et al., 1995), has led to exposure misclassification due to Berkson errors, which increases uncertainty and reduces a study power to identify exposure-response associations (Armstrong, 1998). Furthermore, no JEMs are currently available for IF and RF fields and very little information exists on the levels of exposure to these frequencies in the workplace, or the occupations most at risk.

In order to move research on EMF and health forward, an international team of experts in various areas of epidemiology and occupational hygiene joined forces in the year 2000 to develop a new approach for EMF occupational exposure assessment. This new methodology was expected to be used both to assess the exposure of the subjects in INTEROCC, a spin-off of the INTERPHONE project (Cardis et al., 2007), and to be offered publicly for its use by other researchers. The need was to develop a method that would cover all frequency bands, filling the gap within RF and IF exposures, but also providing new and improved methods for ELF fields which would allow a more individualized exposure assessment and a more accurate assessment of the potential health effects associated with EMF exposures at work, particularly the risks of brain tumours. SMF exposures, although also included in the project, were not the focus of INTEROCC.

## 2.1 The INTEROCC project

INTEROCC is a multinational brain tumour (specifically glioma and meningioma) population-based case-control study, conducted in seven of the countries included in INTERPHONE, a study which focused on the risk of brain tumours and exposure to radiofrequency radiation from mobile phones (Cardis et al., 2007). The INTERPHONE questionnaire provided detailed information not only on the history of mobile phone use and relevant potential confounders, but also on the subjects' occupational history and the use of sources of exposure to EMF in the workplace. The availability of this information provided a unique opportunity to assess brain cancer risk in relation to occupational exposure to EMF.

Subject information was collected using a Computer Assisted Personal Interview (CAPI) questionnaire, for which interviewers were specifically trained. Within the occupational part of the questionnaire, screening questions as well as others more specific were included in order to obtain the maximum level of detail on sources of EMF at work. The INTEROCC relational database

(IRAD) was created with the data collected through the questionnaire, including information on the number and types of sources used by the subjects (or worked nearby) during their working lives as well as usage characteristics (e.g. duration of use, distance to the source, materials being welded/sealed/bonded etc.). Detailed occupational histories for jobs held at least six months were also collected including information on job title, start-stop year etc. The questionnaire was divided in twelve occupational sections covering the most common occupational settings where EMF sources may be present (see Table 1 on the first paper).

The study population includes 2,054 cases of glioma, 1,924 cases of meningioma and 5,601 controls, all recruited between 2000 and 2004. Eligible cases were all residents of the study regions (mainly selected urban centres in Australia, Canada, France, Germany, New Zealand, the United Kingdom and the whole of Israel) with a confirmed first primary glioma or meningioma. Informed consent was obtained for all subjects and all procedures were approved by local Ethics Review Boards (Cardis et al., 2007).

The initial efforts to assess occupational exposures, in all frequencies (from SMF to RF), on the basis of the sources of exposure that the study subjects reported in the questionnaire, involved a preliminary literature review which was carried out to identify documents (articles and technical reports) with measurements for the EMF sources initially identified by a panel of EMF experts, with experience in measuring EMF in occupational settings, and included in the questionnaire. This first literature review led to the construction of an early EMF occupational exposure measurement database (OEMD), which included measurements for many of the sources initially identified by the experts. This database contained 1,424 sets of measurements for 138 EMF sources, extracted from 71 documents. Expert elicitation was also performed for a group of RF sources included in the questionnaire for which no measurement data were identified[i].

# 3. THESIS MAIN AIM AND OBJECTIVES

The aim of this work was to finalize and improve the work started by the INTEROCC Study Group to estimate occupational exposures to electromagnetic fields for study subjects and assess the risk of brain tumours associated with these exposures.

## 3.1 Specific objectives

1. Estimate average electric and magnetic fields exposure to the occupational sources identified in the study, using existing measurement data in the literature, and expert elicitation for sources without available measurements.

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[i] A manuscript with details of the process followed for the expert elicitation were prepared by other members of the project and submitted to the journal Annals of Occupational Hygiene (Bowman et al., 2013) but it is not part of this thesis.

2. Develop individual cumulative estimates of exposure and associated uncertainties for the study subjects over all jobs carried out before the interviews.
3. Study the association between occupational EMF exposure and the risk of brain tumours in the study subjects.

## 4. METHODS AND RESULTS

The project included three well defined phases, for which a different methodology was envisaged in order to achieve the objectives described above. The results of these objectives are three manuscripts, one of them published, one accepted and one to be submitted soon. A fourth manuscript, regarding the development of cumulative indices of EMF exposure for the study subjects, is in preparation.

The results achieved throughout this PhD and included in this thesis, either published on in process of publication, are the following:

**Paper I.** EMF Occupational Exposure Measurement Database

**Paper II.** EMF Source-Exposure Matrix

**Paper III.** Risk of brain tumours (glioma and meningioma) and exposure to RF-EMF or IF-EMF

A fourth paper describing the cumulative algorithms and descriptive statistics for the study population is summarized here as an Appendix.

### 4.1 Estimation of exposure to EMF sources

This phase involved completing the exposure assessment approach developed in INTEROCC, including the following main tasks:

- Identify exposure measurements for the remaining sources included in the questionnaire and, if needed, also for those sources with fewer measurements already available;
- Translate and recode into new source codes all free text entries from the questionnaire responses;
- Locate measurements for the new sources identified in the free text entries;
- Seek the support of EMF experts to assess our confidence on the measurements identified by filling in confidence evaluation forms, including questions on the quality and relevance of these measurements for use in epidemiological studies, in particular in INTEROCC;
- Perform quality controls of the measurements previously collected by reviewing the original documents used.
- Enter newly identified measurements into the database, selected through the confidence evaluation process;
- Develop a methodology to combine and summarize all the measurements in this database in order to create a source-exposure matrix (SEM), containing average estimates of exposure and their variability for all the EMF sources identified.

All these tasks can be summarized in two, the construction of an EMF occupational exposure measurement database (OEMD) with measurements from the literature, and the development of a source-exposure matrix (SEM) by combining the measurements in the OEMD. These two main phases led to the preparation of two manuscripts which describe the construction and content of each of the databases. The methods and results used are described below.

### 4.1.1 EMF Occupational Exposure Measurement Database

First, a quality control of the database with the measurements identified in the initial literature review was carried out by the author of this thesis, by manually reviewing all the papers and technical reports included up to then, making sure that all measurements had been extracted and entered into the database correctly. This early database, which was initially constructed in Excel format, was then rebuilt into Access in order to reduce the possibilities of errors and data loss.  Quality control was performed manually (by the author) and through several automated checks (by another member of the team, JF) in order to avoid errors in the database due to data transfer or unit conversion.

A second literature review was carried out based on the sources identified on the questionnaire´s free text entries as well as for those with fewer numbers of measurements available in the existing OEMD. Various on-line search engines were used (see Paper I) in this review in order to identify additional documents with the required measurements, both published articles and unpublished technical reports. Colleagues involved in occupational EMF measurements were also contacted, who provided documents directly.

A group of EMF experts were asked to perform confidence evaluations of the new measurements collected, assigning a quantitative estimate of the quality and relevance of these measurements and their corresponding paper or report from where they were abstracted based on various predefined characteristics (e.g. sampling strategy, equipment, technique, dosimetry type, accuracy of measurements, anatomical location etc.). The measurements selected were included in the second version of this database.

A final quality control of the revised and updated OEMD was carried out based on electromagnetism relations. These checks were based on the compliance with physical laws such as $B\ [\mu T] = \mu_o\ H\ [A/m]$ (where the permeability of free space $\mu_o = 4\pi \cdot 10^{-7}$ henry/meter). The details of the quality checks were published as supplementary material with the OEMD paper (Vila et al., 2016b).

The resulting OEMD is available in a consultable format on the radiation.isglobal.org website, where conditions for obtaining and using the full database are provided.

The OEMD is on-going effort, as it keeps being updated with newly identified sources and measurement data. As of September 2016, it contains 1,730 sets of measurements (more than 3,000 entries for B-, H-, E-field and Power Density) for 312 EMF sources (i.e. 397 by frequency band).

### 4.1.2 Paper I

Published by Annals of Occupational Hygiene in 2016.

Vila J, Bowman JD, Richardson L, Kincl L, Conover DL, McLean D, et al. A Source-based Measurement Database for Occupational Exposure Assessment of Electromagnetic Fields in the INTEROCC Study: A Literature Review Approach. Ann Occup Hyg. 2016 Mar;60(2):184–204. DOI: 10.1093/annhyg/mev076

### 4.1.3 EMF Source-Exposure Matrix

To construct a source-exposure matrix (SEM), containing exposure estimates (arithmetic and geometric means, maximum values and estimates of variability, SD & GSD) for all the EMF sources in the OEMD by frequency band and dosimetry type, a novel methodology, based on order statistics and the characteristics of log-normal distributions, was developed to summarize the diverse measurement data available. Details of the derivations carried to obtain equations for each data combination in the OEMD can be found in the Supplementary Material for this paper, at the end of the document.

This methodology included the use of the confidence evaluation ratings, previously obtained by EMF experts to assess the quality and relevance, and select the measurements to be included in the OEMD, as weights. This method allowed us to assign more weight to those measurements with higher ratings which were considered more representative for the pooling process. Since the OEMD contains varied measurement data (e.g. means, maximum values, ranges), the combination of these data into a reliable matrix required the development of new mathematical approaches which would allow the use of all the diverse data available. To assess the feasibility of combining measurement data in order to obtain more accurate estimates, and to assess the ability of the SEM to provide sufficient exposure variability between sources several statistical tests were performed (e.g. ANOVA, Levene´s test).

The SEM contains confidence-weighted mean exposure estimates (i.e. arithmetic mean, AM, and geometric mean, GM) and estimates of their associated variability (i.e. standard deviation, SD, and geometric standard deviation, GSD), for all selected sources of EMF by frequency band (SMF, ELF, IF and RF), physical magnitude (B-, H- and E-field) and dosimetry type (e.g. personal, operator position, and spot). Expert judgment estimates included in the OEMD were also used in the pooling and included in the SEM appropriately. Measurements obtained from review articles, from which the dosimetry could not be identified, were also suitably designated also as a special case. In order to use the SEM estimates for subsequent phases of the project, or other epidemiological studies, the following hierarchy was defined to select the most accurate estimates of exposure (i.e. personal, operator position, spot, review, expert judgment).

Since power density (PD) is not well defined in the *near field*, because of its special heterogeneous characteristics, PD values collected from the literature were converted into E- and H-fields, using free space relationships:

$$E[V/m] = \sqrt{PD[W/m^2] * 377\text{ohms}} \tag{3}$$

$$H[A/m] = \sqrt{PD[W/m^2] / 377\text{ohms}} \tag{4}$$

which come from substituting eq. 2 on page 4 into eq. 1 on page 3 (more information on these calculations can be found in the supplementary material of the OEMD and the SEM papers). As an example of the values found in the SEM (Figure 2 of the manuscript), operator position geometric mean electric field levels for RF sources ranged between 0.8 V/m (plasma etcher) and 320 V/m (RF sealer), while magnetic fields ranged from 0.02 A/m (speed radar) to 0.6 A/m (microwave heating).

Quality checks, similar to those carried out for the OEMD, were performed in the SEM, ensuring that both statistical and physical properties were not breached. Details of these quality checks can be found in the articles explaining the methods used for both databases (Papers I and II).

Although initially, we planned to divide the estimates in different SEMs depending on their frequency, it was finally decided to keep them in the same matrix to facilitate their access and use. A manuscript describing this methodology as well as details of the SEM content has been accepted for publication at the Journal of Exposure Science and Environmental Epidemiology (Vila et al., 2016a).

The SEM will be made consultable on the ISGlobal radiation website when the paper is published.  Like the OEMD, the objective is to be able to update the SEM as new information becomes available.

### 4.1.4 Paper II

In press, Journal of Exposure Science and Environmental Epidemiology.

Vila J, Bowman JD, Figuerola J, Moriña D, Kincl L, Richardson L, et al. Development of a source-exposure matrix for occupational exposure assessment of electromagnetic fields in the INTEROCC study. J Expo Sci Environ Epidemiol. 2017 Jul 9;27(4):398–408. DOI: 10.1038/jes.2016.60

## 4.2 Estimation of cumulative exposure of study subjects

The detailed source-based information collected in INTEROCC for each study subject on potential determinants of exposure to EMF at work (e.g. distance, automation, work organization) was used to estimate indices of cumulative EMF exposure by study subject. Algorithms were developed to take into account not only the average exposures in the SEM for the EMF sources reported but also the subject detailed information on how the specific EMF sources were used or how exposure occurred because of work in the proximity.

The additional information obtained during the interviews such as duration and frequency of use, distance to the source and other exposure modifiers was used to design these exposure algorithms. The available information from the occupational histories (e.g. job title, job description, company name/description, start-stop year) was also used in order to achieve a more accurate assignment of exposures. For each occupational section, a flowchart had been constructed including the possible responses that could be obtained from the subjects. These flowcharts were used in the development of the cumulative exposure algorithms to ensure that all possible scenarios were covered. The algorithm's output is the cumulative exposure to electric or magnetic fields for each of the frequency bands over all jobs in a subject's occupational history.

Initially, cumulative exposure algorithms were developed for each of the twelve INTEROCC occupational sections. However, for the purpose of this thesis, seven of them (i.e. radars, telecommunication antennas, transmitters, food heating, industrial heating, semiconductors manufacturing and diagnosis and treatment), in which RF and/or IF EMF sources are commonly used, were finalized and used to estimate cumulative exposures for the study subjects in these frequencies.

Uncertainties in the questionnaire responses due to errors in the collection of the subject’s information (e.g. missing data on dates, etc.) were also addressed. For instance, in the cases where subjects provided ranges, we took the mid-point. A full uncertainty propagation will be the conducted in a future paper on risk. A manuscript describing the algorithms and summary descriptive of the results obtained is under preparation. This manuscript will include the calculation of uncertainties as well as sensitivity analyses, using the lower and upper bounds of ranges and other imputed data. Details of the work performed so far are described in the Appendix.

### 4.3 Estimation of risk of brain tumours and occupational exposure to RF or IF EMF

The main goal of this phase was to assess whether exposure to EMF in occupational settings can increase the risk of brain tumours within the study subjects. Descriptive univariate analyses were carried out to characterize the distributions of exposure among cases and controls. Multivariate conditional logistic regression models were used to estimate the odds of developing glioma or meningioma as a function of cumulative exposure to occupational RF or IF EMF. Models were stratified by country, region, sex, and five-year age groups and adjusted for level of educational attainment (high school or less, medium level technical or professional school, university graduate).

The main analysis used categorical indicators of cumulative exposure as the predictor variable, examined overall (1-year lag) and in different exposure-time windows selected a priori, 1-4, 5-9, 5+ and 10+ years before the diagnosis or reference date. Analyses using exposure as a continuous variable and testing for nonlinearity in response were also conducted.

Other information collected in INTERPHONE, in addition to the occupational information considered here, about other potential risk factors for brain tumours including mobile phone use, use of other wireless communication devices (e.g. cordless telephones), exposure to ionizing radiation, smoking, and the subjects´ personal and familial medical history, were used to assess the effect of these factors as potential confounders of the association between occupational EMF exposure and risk of brain tumours.

Factors were systematically included in the risk models if they produce a change of 10% or more in the risk estimates. To control for the major a priori confounding factors (i.e. sex, age and study region) individually or frequency-matched controls were randomly selected from the source population and conditional logistic regression was based on groups defined by these factors.

Sensitivity analyses were conducted excluding proxy interviews, participants with a poor quality interview, participants older than 60 years of age, or with a history of neurofibromatosis or tuberous sclerosis. Potential effect modification by study country, sex, level of educational attainment (high school or less vs greater than high school), age at reference date (<50 vs 50+ years), and cigarette smoking status (never vs ever), and other RF-EMF exposures (i.e. mobile phones) was assessed by entering product terms into conditional logistic regression models and assessing their significance according to the likelihood ratio test.

## 4.4 Paper III

To be submitted in 2016.

Vila J, Bowman JD, Figuerola J, Gracia E, Kincl L, Richardson L, Cardis E, on behalf of the INTEROCC Study Group. **Occupational exposure to high frequency electromagnetic fields and risk of brain tumours in the INTEROCC study**. To be submitted.

# Occupational exposure to high frequency electromagnetic fields and risk of brain tumours in the INTEROCC Study

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Abbreviated title: high-frequency EMF and risk of brain tumours

Word count - Abstract: 323
Word count - Main text: 5,036
Total number of tables and figures: 10

Financial support: This work was funded European Commission grant 603794 (GERoNiMO project). The conduct of the INTEROCC study was funded by the National Institutes for Health (NIH) Grant No. 1R01CA124759-01. The work on the French occupational data was in part funded by AFSSET (Convention N° ST-2005-004). The INTERPHONE study was supported by funding from the European Fifth Framework Program, 'Quality of Life and Management of Living Resources' (contract 100 QLK4-CT-1999901563) and the International Union against Cancer (UICC). The UICC received funds for this purpose from the Mobile Manufacturers' Forum and GSM Association. Provision of funds to the INTERPHONE study investigators via the UICC was governed by agreements that guaranteed INTERPHONE's complete scientific independence (http://interphone.iarc.fr/interphone_funding.php). In Australia, funding was received from the Australian National Health and Medical Research 5 Council (EME Grant 219129) with funds originally derived from mobile phone service licence fees; a University of Sydney Medical Foundation Program; the Cancer Council NSW and The Cancer Council Victoria. In Montreal, Canada, funding was received from the Canadian Institutes of Health Research (project MOP-42525); the Canada Research Chair programme; the Guzzo-CRS Chair in Environment and Cancer; the Fonds de la recherche en santé du Quebec; the Société de recherche sur le cancer; in Ottawa and Vancouver, Canada, from the Canadian Institutes of Health Research (CIHR), the latter including partial support from the Canadian Wireless Telecommunications Association; the NSERC/SSHRC/McLaughlin Chair in Population Health Risk Assessment at the University of Ottawa. In France, funding was received by l'Association pour la Recherche sur le Cancer (ARC) (Contrat N85142) and three network operators (Orange, SFR, Bouygues Telecom). In Germany, funding was received from the German Mobile Phone Research Program (Deutsches Mobilfunkforschungsprogramm) of the German Federal Ministry for the Environment, Nuclear 45 Safety, and Nature Protection; the Ministry for the Environment and Traffic of the state of Baden-Wurttemberg; the Ministry for the Environment of the state of North Rhine-Westphalia; the MAIFOR Program (Mainzer Forschungsforderungsprogramm) of the University of Mainz. In New Zealand, funding was provided by the Health Research Council, Hawkes Bay Medical Research Foundation, the Wellington Medical Research Foundation, the Waikato Medical Research Foundation and the Cancer Society of New Zealand. Additional funding for the UK study was received from the Mobile Telecommunications, Health and Research (MTHR) program, funding from the Health and Safety Executive, the Department of Health, the UK Network Operators (O2, Orange, T-Mobile, Vodafone, '3') and the Scottish Executive. All industry funding was governed by contracts guaranteeing the complete scientific independence of the investigators. MCT was funded by a Canadian Institutes of Health Research Fellowship.

Conflict of interest: The authors have no conflicts of interest to declare.

## ABSTRACT

Introduction: The possible association between brain tumours and exposure to high frequency electromagnetic fields is still inconclusive. The incidence of this serious disease differs by country and, overall, is higher in men suggesting a possible occupational origin. This study aimed to assess the possible association between occupational exposure to radiofrequency (RF) and intermediate frequency (IF) EMF and risk of glioma and meningioma, using the large dataset of subjects in the INTEROCC study and the novel exposure assessment methodologies developed within the project. Methods: Mean estimates of exposure from the source-exposure matrix (SEM) created in INTEROCC, together with the detailed individual occupational information collected on EMF sources, such as duration and conditions of use, were used to obtain individual estimates of EMF cumulative exposure. Cumulative exposure estimates for RF and IF EMF were used to assess occupational exposure and risk of brain tumours (glioma and meningioma), using conditional logistic regression, based on exposed subjects' categories and using exposure continuously. Results: Overall, there was no association between glioma or meningioma risk and cumulative exposure to RF EMF, although some positive associations were identified in the highest exposed groups in the 1- to 4-year exposure window for glioma and in all windows for meningioma. A positive linear association was also found for both tumour types using exposure as a continuous variable. For IF EMF, weak positive associations were found in the most recent time windows for glioma in the highest exposed groups, although the small number of exposed subjects available for this analysis makes the interpretation of these results difficult. Conclusion: The risk estimates obtained for glioma and recent RF and IF EMF exposures might reflect a possible role of high frequency EMF in the later stages of carcinogenesis (promotion and progression). However, the lack of association overall and the small number of subjects available for some of the analyses weaken the strengths of our results. Further studies are warranted, both using and improving our methods.

## INTRODUCTION

The incidence of central nervous system tumours worldwide is largely heterogeneous and trends for different tumour types are still under discussion due to the diverse quality of cancer registries and the lack of complete reporting of cases.[1,2] However, increases in the incidence of brain cancer overall have been noted since the late 1970s and early 1980s in many industrialized countries. Although this could reflect a true increase, it could be mainly due to improved diagnostic capabilities over the last decades, resulting in a more complete reporting of specific tumour types.[1,3–7] Glioma and meningioma are the most frequent brain tumour types in adults, the former representing 81% of all malignant brain tumours.[5,8,9] Gliomas are originated in the glial tissue and are mostly malignant tumours.[9] Meningiomas are commonly benign, although there are some rarer malignant subtypes.[8]

The aetiology of this very serious disease remains largely unknown. The only two widely accepted risk factors, ionizing radiation and genetic disorders, account for a small portion of cases. The evidence for other possible risk factors, such as non-ionizing radiation and certain chemicals, is inconclusive.[5,10–12] However, recent years have seen an increasing number of studies showing positive associations for both radiofrequency (RF) and extremely-low frequency (ELF) electromagnetic fields (EMF). For non-occupational exposures, studies on mobile phones – the largest source of exposure for the general public – have not provided evidence of an increase in glioma and meningioma risk, overall, although increased risks were observed in some studies among heavy users and/or long-term exposures.[13] Other studies have investigated cancer risks in the proximity of radio and television transmitters with inconclusive evidence. For occupational exposures, some authors looked at RF exposures such as those affecting radar technicians, radio and telegraph operators, plastic sealers or embassy personnel.[14–16] Although some increases were reported, these were inconsistent and studies had many limitations, specially poor or no exposure assessment and small sample sizes.[14–19] For intermediate frequency (IF) fields, the number of studies is very limited and there is inadequate evidence about any possible association with brain tumours.[20]

Most of the previous studies on RF and/or IF EMF and brain tumours used surrogates of exposure, such as distance to the source, job title, use of communication devices, and other group classifications. Very few studies have used quantitative exposure metrics. Those that did, have mainly focused on estimates of the amount of RF energy absorbed, from use of mobile communication devices, measured as specific energy absorption rate (i.e. SAR), or cumulative absorbed energy.[21,22] Some studies used measurements to validate modelled estimates,[23] which in general showed better correlation than with simple measures based on amount use of mobile devices. However, most of the recently obtained measurements based on RF dosimeters have not been used yet for epidemiological analysis. In occupational studies, work was mainly based on the use of specific job titles or groups of workers thought to be exposed to RF fields, using occupational histories and/or tasks and qualitative exposure estimates assigned from hygienists[24] or a job-exposure matrix.[25] Only a few studies involving military personnel[17–19,26] radio and telegraph operators[15] or embassy employees[14] made use of measurements of RF field intensities. These limitations, particularly on the exposure assessment methods used, may have affected the results of the studies, reducing their ability to find true associations or differences for the cancers studied, including brain tumours, if they exist.

The International Agency for Research on Cancer (IARC) classified RF as possibly carcinogenic to human (group 2B), based on *limited epidemiological evidence*, mostly on mobile phone and brain cancer, and *limited experimental evidence,* mainly based on co-carcinogenicity experiments.[13] Many *in vivo* or *in vitro* studies have been undertaken but consistent effects have only been observed with exposures that increased whole body or localised tissue temperature by a degree or more, which is well above the existing guidelines for RF exposure.[27] Several mechanisms have been proposed which could be responsible of EMF effects on health, including thermal and non-thermal processes (e.g. absorbed energy,[23] reactive oxygen species,[28] or activation of voltage-gated calcium channels[29]). Recently, preliminary results of a large-scale new animal experiment identified an increased rate of glioma and schwanoma in rats[30], as well as indications of RF induced DNA damage, which are still unpublished but could confirm previous similar results.[31,32] Mechanistically, several carcinogenicity studies have proposed the role of RF fields in the promotion/progression phase of tumour development.[33–36] However, to our knowledge, few studies have investigated this hypothesis, which requires the analyses of different exposure windows and, therefore, large scale studies.

Within the framework of the INTEROCC project, a source-based occupational exposure measurement database (OEMD) was constructed for the EMF sources identified in the study.[37] This database was the basis to construct a source-exposure matrix (SEM), involving confidence-weighted estimates of exposure for all the EMF sources in the OEMD.[38] The aim of this work is to use the SEM estimates to analyse the possible association between occupational exposure to sources of RF or IF EMF and the risk of brain tumours, specifically glioma and meningioma in the INTEROCC population. The detailed information collected for cases and controls on the use of occupational sources of EMF and complementary information (e.g. work organization, distance to the source), together with the novel exposure assessment methodology developed within the project, provides an opportunity to assign detailed quantitative estimates of high frequency EMF exposures to all study subjects and to evaluate the risk of brain cancer in a large population-based study. The size of the study allows, in particular, the investigation of potential effects from cumulative exposure both overall and in specific exposure time windows.

## MATERIALS AND METHODS

### *Study Population*

The INTEROCC study comprises data from seven of the thirteen countries included in the international case-control study on mobile phone use and brain cancer risk, INTERPHONE.[39] In these countries, detailed occupational histories were obtained from study subjects and occupational hygienists were available to assist in the coding of occupations. Details of the study design have been published[39]. Briefly, the study was population based in all participating countries. Incident cases of primary brain (i.e. glioma and meningioma), acoustic neurinoma and salivary gland tumours were identified between 2000 and 2004 in all participating hospitals in the study regions: areas of Australia, Canada, France, Germany, New Zealand and the United Kingdom, and on a national scale in Israel. Extensions of age limits were carried out in Germany (up to 69 years), Israel (18+ years) and the United Kingdom (18-69 years), to allow greater case ascertainment. The core

INTERPHONE protocol included cases aged 30 to 59 years of age, the age range of most concern, at the time, for the study of effects of mobile phones. Several countries chose to include cases from a broader age group, up to 69 years in Germany, 18 years and above in Israel and 18 to 69 years in the United Kingdom, which were all included in the INTEROCC study.

Controls were randomly selected from population registries and electoral lists, depending on the country, patient lists in the UK and, in the region of Ottawa (Canada), through random digit dialling. All controls were either individually or frequency matched to the cases by age (5-year groups), sex, centre and country. Although the initial study design included the selection of one control per glioma or meningioma case, all eligible controls were used in this work to maximise statistical power. The reference date for controls was based on the median difference between diagnosis and interview date for all cases by study centre, which was subtracted from the control interview date. All cases and potential controls identified were contacted, informed about the study and asked whether they wanted to participate. For subjects who agreed, a signed informed consent was obtained previous to the interview process.

In total, occupational data was collected for 3,978 cases of brain tumours (i.e. 2,054 gliomas and 1,924 meningiomas) and 5,601 controls in the 7 INTEROCC countries. The most frequent reasons for non-participation were refusal (64%) and inability to contact (27%). Participation among glioma cases for low- and high-grade tumours was similar (i.e. 71% and 67%, respectively). Ethics approval was obtained from the Ethics Committee of the International Agency for Research on Cancer (IARC) and appropriate ethics committees in all participating countries for the INTERPHONE study and from the Ethics Committee of the Municipal Institute for Medical Investigation (IMIM) in Barcelona, for use of the anonymised INTERPHONE and INTEROCC data.

### *Data Collection and Cleaning*

The main aim of INTERPHONE was to assess the association between mobile phone use and the risk of benign and malignant brain tumours. However, a detailed occupational section was developed within the core study questionnaire, in order to collect information on possible confounders and examine other etiologic hypotheses. Subject information was collected through a computerized assisted personal interview (CAPI) system. Only a few subjects were interviewed by telephone, while proxy respondents were allowed if the original participant died or was unable to participate. After the collection of a brief occupational history, a positive response to any of a list of screening questions allowed the interviewer to focus on sources and tasks that could involve the highest levels of occupational EMF exposure. Thus, specific questions were used about particular EMF sources (such as radars, RF sealers, or microwave diathermy devices).

All EMF sources were classified within twelve occupational sections, involving sources with different frequencies (from 0 Hz to 300 GHz). The questionnaire was repeated if the subject reported work in more than one of these twelve occupational sections (see Appendix I from the first article of this series[37] for a detailed description of the screening questions and occupational sections). Complementary information on tasks and work environments included distance to the source, material being welded/heated/bonded, as appropriate, start and stop years of use or in proximity to the sources, and the number of hours per week/month in which exposure occurred. A full occupational history was also collected for all jobs held for at least six months, including job title, start and stop date, and company name and description. This information was compiled, together with the rest of the data collected in the main study, into the INTERPHONE relational database (IRAD).

The quality of the information on the specific EMF sources reported was assessed through comparisons with the data collected in the full occupational histories. Errors identified, such as incongruent dates or responses not obeying the questionnaire logic, were corrected when possible. Imputation of missing data was performed using average or median values from the controls. Subjects for which imputation was difficult to achieve with minimal guarantees were excluded from the analysis. Although other definitions for high frequency EMF exist,[40] within the INTEROCC project, radiofrequency (RF) EMF were defined as the range between 10 MHz-300 GHz, while intermediate frequency (IF) EMF were considered between 3 kHz-10 MHz. In this paper, we consider high frequency fields those with frequencies above 3 kHz.

### *Exposure Assessment*

The SEM was used to assign average exposure levels for each source reported by the study subjects on the basis of the RF and/or IF sources reported in the questionnaire. Of the twelve occupational sections, seven of them (i.e. radars, telecommunication antennas, transmitters, semiconductors manufacturing, medical diagnosis and treatment, and industrial and food/dental heating) entailed work with sources of RF and/or IF EMF. For each of these sections, specific cumulative exposure algorithms were developed involving the use of the information on exposure duration and rate as well as average levels (i.e. AM) of E-field exposure associated with each of the EMF sources reported. Since the most relevant exposure metric, if any, for the carcinogenicity of RF and IF EMF is not known,[41] and RF and IF sources reported by the subjects involved different frequencies (from several kHz to several GHz), and following the recommendations of the International Commission on Non-Ionizing Radiation Protection (ICNIRP), averaged E-field levels in the SEM were converted to ICNRIP ratios by dividing the mean estimates by the reference levels associated with each frequency band.[27] Squared ICNIRP ratios – to consider energy rather than incident field –, together with the subjects information collected on determinants of exposure (e.g. distance to source, automation) were used to calculate indices of cumulative RF and IF EMF. Details of the cumulative exposure algorithms used and calculation of the ICNIRP ratios will be published elsewhere.

The mean (SD) number of sources per subject was 1.33 (0.83) for glioma cases and 1.31 (0.65) for meningioma cases, and 1.35 (0.92) for controls. A small number of subjects (n=365) were excluded in this phase because of the lack of information on sources or duration/rate. Figure 1 shows the distribution of subjects excluded in each phase. A total of 1,943 glioma cases, 1,857 meningioma cases, and 5,381 controls were finally included in the analysis. Of the subjects excluded, 365 were lost because of the impossibility to assign a source(s) while 33 subjects had missing data on education.

### *Statistical Analysis*

Conditional logistic regression models were used to calculate adjusted Odds Ratios (ORs) and 95% confidence intervals (CIs) for the association between occupational cumulative exposure to RF or IF EMF and risk of glioma or meningioma. For this analysis, we used the combined data from the seven INTEROCC countries. Models were stratified by sex, age (5-year groups), region and country, and adjusted by education. The effect of exposure was modelled both using categorical and continuous variables of exposure. For the categorical analyses of RF E-field cumulative exposure, fixed cut points were decided *a priori*, based on the distributions of cumulative exposure of controls. For IF, due to the small number of exposed subjects available, categories were created based on the median cumulative H-field exposure of controls. Lifetime cumulative exposure (1-year lag), cumulative exposure at 5- and 10-year lags, as well as two exposure time windows defined *a priori* (i.e. 1 to 4, and 5 to 9 years before the diagnosis/reference date), were assessed. These time windows were chosen to test the possibility that RF and or IF EMF may play a role in the promotion/progression of tumours; if this were the case, one would expect more recent exposures to entail higher risks than exposures received further in the past. The reference category for the main analyses included only subjects never exposed to RF or IF EMF at work. For the continuous analyses, a linear exposure response both for cumulative exposure to RF E-fields or IF H-fields was modelled, as well as, to assess departure from linearity, models using polynomials in exposure with log transformations, such as:

$$\operatorname{logit}(Y) = \beta_0 + \beta_1 * X + \text{covariate(s)}$$

$$\operatorname{logit}(Y) = \beta_0 + \beta_1 * \ln(X) + \text{covariate(s)}$$

$$\operatorname{logit}(Y) = \beta_0 + \beta_1 * X + \beta_2 * X^2 + \text{covariate(s)}$$

$$\operatorname{logit}(Y) = \beta_0 + \beta_1 * \ln(X) + \beta_2 \ln^2(X) + \text{covariate(s)}$$

The adequacy of the models were evaluated using the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC).[42] Confidence intervals for the models using the continuous exposure data were calculated using the profile likelihood from each model.

Potential confounding by cigarette smoking, exposure to ionizing radiation, allergy history, and mobile phone use were also examined. Sensitivity analyses were performed by excluding proxy interviews, participants who were judged by the interviewers as not collaborative, participants >60 years of age, and participants with a history of neurofibromatosis or tuberous sclerosis, as well as for high- and low-grade glioma types, separately. Potential effect modification by age, sex, country and education was assessed by including an interaction term between exposure and these variables and assessed using the likelihood ratio test.[23] All analyses and graphics were performed using the open source R software, version 3.2.3.[43] Regression models were created using the "clogit" function from the "survival" package.[44] Profile likelihood confidence intervals were calculated with Stata 14 software.[45]

## RESULTS

Table 1 shows the characteristics of the cases and controls in the study. Meningioma cases tended to be slightly older on average than glioma cases, and 74% were women, compared to 40% for glioma. More glioma cases reported working with transmitters and telecommunication antennas than meningioma cases or controls. More meningioma cases reported working with sources for heating food than glioma cases or controls.

Table 2 shows the distribution of cumulative levels of exposure of exposed cases and controls. Median RF E-field overall exposure (1-year lag) was slightly higher in glioma than meningioma cases who had similar levels than controls. For IF H-fields, median overall levels for meningioma cases were similar to those of controls, while glioma cases had lower exposure levels. Because of the highly skewed nature of the exposure distribution, mean levels were much higher, with very large standard deviations. Extreme maximum values were especially evident when considering overall exposure (1-year lag). Around 90% of the subjects were not exposed either to RF E-fields or IF H-fields. The RF and IF sources most frequently reported were "walkie talkie" and "induction heater", respectively. The sources reported with the highest levels of exposure were "RF sealers/welders for plastic & rubber", for RF, and "Electronic Article Surveillance (EAS) system", for IF (Table 3).

There was no clear evidence for an association between cumulative exposure (squared ICNIRP ratio-year) to RF E-fields and glioma risk overall (1-year lag) or in any of the other exposure lags and time windows, using the categorical classifications of cumulative exposure (Table 4). In this analysis, slightly reduced ORs were identified in nearly all groups; a significantly reduced OR was found in the 0.1≥-1.00 category of exposure overall and in analyses with a 5-year lag for glioma. For both glioma and meningioma, a non-significantly increased OR was seen only in the 5.00≥-10.0 category in the analyses with a 1- to 4-year lag. For meningioma, the OR in the highest exposure category was also increased in analyses with 5 and 10-year lags. There was no clear trend in most groups. Only in the 1- to 4-year window for glioma there was a distinct pattern of increased risk with increasing level of exposure, although risk estimates obtained for this group were not statistically significant, OR for highest exposed group 1.17 (95% CI 0.62-2.21). Analyses restricted to men (Table 8), showed similar results for glioma. For meningioma, an increased OR was seen in the highest exposure category in all time windows and lags. It was highest in the 1-4 years before diagnosis OR 2.02 (95% CI 0.75-5.39) and a trend was seen with increasing exposure in the 5- to 9-year time window. Numbers of exposed cases in women were too small for meaningful analyses.

In the continuous analysis, a statistically significant positive linear association (OR=1.01, 95% CI 1.00-1.02, for a 1 point change in the squared ICNIRP ratio-year, LRT p-value=0.02) was found for cumulative exposure to RF E-field and risk of glioma for the 1- to 4-year exposure time window (Table 5). No association was seen in this analysis for exposure overall (1-year lag) or other exposure windows (not shown). Analyses using polynomials and/or log transformations did not improve the fit. Figure 2 shows the exposure-response association from predicted risk estimates using the continuous exposure data (1- to 4-year window) and two of these models (log-linear and translog-quadratic, the latter based on log transformation of exposure, both in the linear and the squared terms). This figure also shows the OR estimates and 95%CI for the categorical analysis for the same exposure window.

For meningioma, little association was seen overall, though a positive association was also seen in the 1- to 4-year time window in males OR 1.0, 95% CI 1.00-1.06 for a 1 point change in the squared ICNIRP ratio-year. Analyses of different transformations showed no evidence of departure from linearity of the exposure response relationship.

For IF, a weak positive association between H-field cumulative exposure (squared ICNIRP ratio-year) and risk of glioma was identified in the highest exposed group for 1- to 4-year and 5- to 9-year exposure time windows (Table 7). However, these associations were not statistically significant and based on a small number of subjects available. No other positive associations were identified in any other exposure windows or using cumulative exposure overall (1-year lag) for both glioma and meningioma.

In the sensitivity analysis, little change was seen (results not shown) for glioma or meningioma when using the lowest exposed group rather than the unexposed group as the reference category, when removing subjects above 60 years of age or excluding subjects with very high exposures (above 99th percentile of cumulative exposure). Removal of unresponsive subjects did not change the results by more than 10%.

## DISCUSSION

This study, based on the analysis of 1,943 and 1,857 cases of glioma and meningioma respectively and 5,381 controls is the largest case-control study of brain tumours and occupational RF and IF exposure to date. The work on exposure assessment, based on a detailed source based questionnaire and the use of a source exposure matrix specifically developed for the project is, to our knowledge, the most in depth effort aimed at estimating exposure from RF and IF in an epidemiological study. The study showed no clear evidence for an association between either RF or IF cumulative exposure and risk of either glioma or meningioma overall or in separate time windows. However, weak positive associations were identified in both the categorical and the continuous analysis for RF E-fields, especially in the 1- to 4-year exposure window for glioma and in all time windows for meningioma. These positive associations were slightly clearer when analysing male subjects separately, particularly for meningioma. The number of exposed women was too small for meaningful analyses. In general, there were more negative than positive associations in all exposure windows, mostly not statistically significant. In the categorical analysis, positive associations were mostly identified in the highest exposed groups. For IF H-fields, associations were also mostly negative and not statistically significant. Some positive associations, also non-statistically significant, were identified in the highest groups of exposure for glioma but not for meningioma.

Our findings are in agreement with some recent and older studies looking at exposure to RF fields and both brain and all cancer types. Studies focusing on all cancer types have had heterogeneous results. While most of them[14,18,26,46,47] did not find positive associations, few studies used exposure measurements to assess the risk of cancer incidence. A study of female radio and telegraph operators,[15] for instance, in which RF spot measurements were performed and used for the analysis, found a slight non-significant increase in all cancer types in comparison with the general population. An Italian study[16] investigating cancer risks among plastic-ware workers exposed to RF-EMF found a standardized mortality ratio of two fold, for malignant neoplasms. However, these results had wide, non-significant confidence intervals and a small number of subjects. Another cancer mortality study performed on mobile phone manufacturing workers,[17] in which a job-exposure matrix was used to assign semi-quantitative exposure estimates to the study participants found no increased risks for the highly exposed groups.

Although most of the above studies included cases of brain cancer among their subjects, only a few of them[26,46,47] had sufficient numbers to be considered informative. A non-significant increase of brain cancer risk (SMR 1.8, no CI provided) was found in the study of radio operators,[46] while the studies on police officers and naval and aviation personnel found non-statistically reduced risks for brain tumours; these studies did not, however, look at risk by level of exposure. Two case-control studies looked at exposures to RF fields and brain cancer. In one of them,[48] semi-quantitative exposure estimates were assigned to male air force workers based on a detailed occupational history obtained through questionnaire. Although no association was found for exposure level and risk of brain cancer, a small excess risk was seen when comparing ever versus never exposed. The other case-control study,[49] in which exposure of workers in various occupations were classified by expert industrial hygienists, found a significant increase risk among men exposed for more than twenty years. A study in Australia in which researchers looked at glioma and RF exposure,[19] using a general job-exposure matrix (JEM), found many reduced ORs. It is not clear at present how appropriate a JEM is for assessment of occupational RF exposure given the vary great variability of exposure within job categories, depending on sources used.[23]

More recently, a German study[24] used some of the data collected within the INTERPHONE project to classify the subjects according to their likelihood of exposure to RF. This study found no significant association for occupational exposure to RF and risk of brain cancer. The OR for glioma in highly exposed subjects was 1.22 (95% CI 0.69-2.15) overall and 1.39 (95% CI 0.67-2.88) when only high exposure for more than ten years was considered. Similar results were obtained for meningioma, with an OR for exposure overall of 1.34 (95%CI 0.61-2.96) and 1.55 (95%CI 0.52-4.62) for ten years or more of high exposures. The results we obtained with the categorical analysis are similar, with not-significantly increased risks for highly exposed groups and indications of an exposure response relationship in the continuous analyses. Although the number of subjects in our study was considerably larger than the previous studies, most subjects had no exposure and hence the statistical power of our study is still limited.

There are only a few studies in the scientific literature which focused on occupational exposures to high frequency electric and magnetic fields and risk of brain cancer.[50] However, the literature on extremely-low frequency (ELF) EMF and health outcomes, in particular brain tumours is extensive. A recent study on occupational ELF magnetic fields and brain tumours[51] found a statistically significant association in the 1- to 4- year exposure window for glioma. These findings and the results of our own analyses support the hypothesis that EMF might be a cancer promoter, and therefore could play a role within the last phases of carcinogenesis (i.e. promotion and progression).[33–36]

Very little information exists in the literature regarding exposure to high frequency magnetic fields (H-fields) and risk of brain or other cancer types[20,33,52]. We decided to analyse IF H-fields rather than E-fields because in many IF sources, such as in electronic article surveillance (EAS) systems and RF IDs, the magnetic component is usually more important.[53,54] Our findings do not support a clear association between exposure to IF H-fields and glioma or meningioma. However, weak non-significant increased risks were identified in the highest exposure groups for glioma. The small number of exposed subjects available for this analysis makes the interpretation of these results difficult.

For our risk analyses, we used the traditional categorized approach together with a continuous analysis based on polynomials. Although fractional polynomials have been upheld by some authors as the ideal approach to model continuous covariate data, classical polynomials are considered the natural extensions of categorical analysis.[55] We decided to use classical polynomials to compare the results obtained using the straight line (i.e. log-linear model). Since this model provided the best fit for our data, given the results of the other models which obtained higher AIC and BIC values, we decided against trying more complicated models, following the parsimonious principle. AIC and BIC are classical methods for models selection for models based on maximum log-likelihood.[56] Those models which obtained the lowest values for AIC and/or BIC were thought to have the best goodness of fit. These tests showed that the most parsimonious model, the straight line, considered the best fit values. The linear model was also more prone to obtain statistically significant confidence intervals, especially when considering the shape of the likelihood function. For this reason, confidence intervals for the OR obtained with continuous models were calculated using the actual profile likelihood of the models. Profile likelihood-based confidence intervals provide more accurate estimates when modelling highly skewed distributions,[57,58] such as our cumulative exposure data.

Another drawback associated with categorical analysis is the necessity to select cut points,[55] either based on previous publications or, empirically, on the actual distributions of the data. Because of the characteristics of the distribution of our exposure data, we decided to use fixed cut-points based on the overall exposure distribution among controls in an effort to distribute the categories widely throughout the distribution as much as possible. As a sensitivity analysis, we used cut-points based on quantiles of exposure, as recently recommended for skewed distributions such as EMF data.[41] The results using these cut-points were similar to those using the original fixed categories. Furthermore, the use of fixed cut-points allows for the comparison between categories while exposure groups based on quantiles makes this comparison more difficult.

Because the biophysical mechanism(s) by which RF and/or IF EMF may damage health are not known,[33,40,59,60] and heating is the only well-established effect for RF-EMF, specific absorption rate (SAR) and other dose metrics have been commonly used in epidemiological studies as the preferred measure of exposure/dose. However, dosimetric modelling should not substitute traditional exposure-response analysis,[61] since bad exposure data cannot be improved by estimating dose. Although there is no evidence to support that frequency-adjusted EMF based on ICNIRP reference levels could be a good exposure metric, this could be correlated with the disease, since the coupling and distribution of RF and IF fields in the body, in the form of quantities such as induced electric and magnetic fields, power deposition or energy absorption, are determined by the characteristics of the source and its frequency.[40,62]

The use of squared ICNIRP ratio-year as the selected exposure metric for our analyses was based on the necessity to adapt the incident fields (either RF E-fields or IF H-fields) to the actual frequency of the source, since subjects in INTEROCC reported the use/exposure of more than one source. Following the recommendations of the International Commission on Non-Ionizing Radiation Protection[27] and previous efforts to estimate cumulative exposure to RF or IF fields,[63] the levels of exposure for each reported source were transformed into ICNIRP ratios which were then squared before adding the levels from various sources. This methodology allows taking into account the different frequencies of the sources pooled as well as considering energy rather than incident field. An Italian study[16] in which an increased risk of malignant neoplasms was found for plastic-ware workers exposed to RF-EMF, also identified that the corresponding ICNIRP limit recommended at the time, 10 $W/m^2$, was frequently exceeded.  The use of ICNIRP adjusted cumulative exposure estimates provides a new approach for the assessment of cumulative exposure to multiple sources of exposure with different frequencies over time, a field for which very little literature exits until now. Although the results of this study are not conclusive, future studies are warranted making use of this and similar approaches as well as of the source-based methodology developed in INTEROCC.

TABLES AND FIGURES

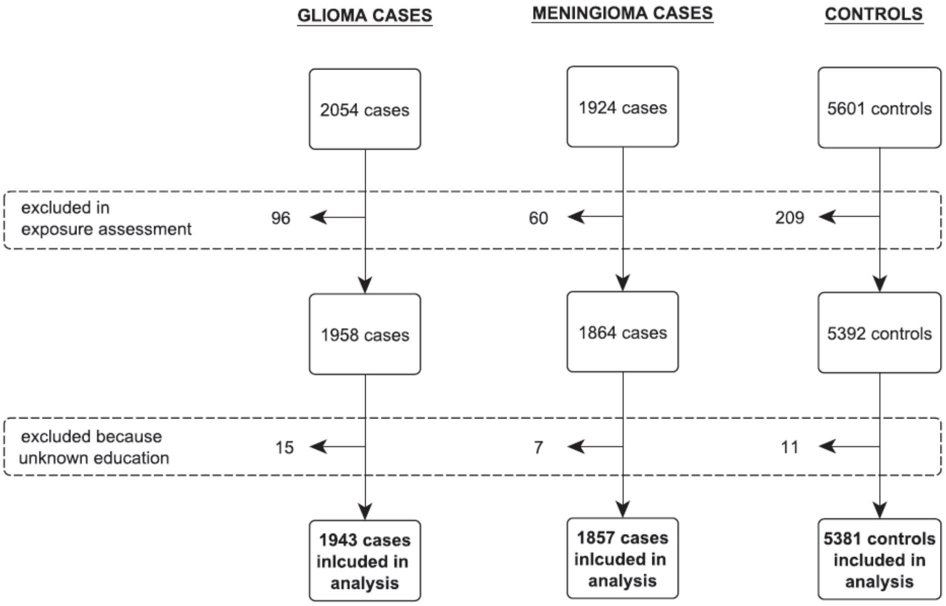


Figure 1. Flowchart of subjects included and excluded in the analysis of RF and IF EMF occupational exposure. INTEROCC study. Data from Australia, Canada, France, Germany, Israel, New Zealand, and United Kingdom, 2000-2004.

Table 1. Distribution of cases and controls with information on occupational RF and/or IF EMF sources by age, education, country, and occupational section. INTEROCC study. Data from Australia, Canada, France, Germany, Israel, New Zealand, and United Kingdom, 2000-2004.

| | **Glioma cases** | | **Meningioma cases** | | **Controls** | |
|---|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **n** | **%** |
| | 1,943 | 100 | 1,857 | 100 | 5,381 | 100 |
| Age[a] | | | | | | |
| <35 | 216 | 11% | 82 | 4% | 414 | 8% |
| 35-39 | 171 | 9% | 96 | 5% | 452 | 8% |
| 40-44 | 215 | 11% | 166 | 9% | 623 | 12% |
| 45-49 | 240 | 12% | 266 | 14% | 728 | 14% |
| 50-54 | 346 | 18% | 369 | 20% | 949 | 18% |
| 55-59 | 310 | 16% | 319 | 17% | 993 | 18% |
| 60-64 | 192 | 10% | 189 | 10% | 501 | 9% |
| 65-69 | 137 | 7% | 170 | 9% | 434 | 8% |
| 70+ | 116 | 6% | 200 | 11% | 287 | 5% |
| Sex | | | | | | |
| Male | 1,163 | 60% | 483 | 26% | 2,348 | 44% |
| Female | 780 | 40% | 1,374 | 74% | 3,033 | 56% |
| Education[b] | | | | | | |
| High school or less | 1,031 | 53% | 1,120 | 60% | 2,912 | 54% |
| Medium-level technical school | 378 | 19% | 357 | 19% | 1,001 | 19% |
| University | 534 | 27% | 380 | 20% | 1,468 | 27% |
| Country | | | | | | |
| France | 90 | 5% | 143 | 8% | 463 | 9% |
| Germany | 353 | 18% | 374 | 20% | 1504 | 28% |
| Israel | 419 | 22% | 722 | 39% | 958 | 18% |
| United Kingdom | 557 | 29% | 237 | 13% | 1,031 | 19% |
| Australia | 282 | 15% | 239 | 13% | 642 | 12% |
| Canada | 162 | 8% | 92 | 5% | 625 | 12% |
| New Zealand | 80 | 4% | 50 | 3% | 158 | 3% |
| Occupational section | | | | | | |
| Transmitters | 306 | 49% | 133 | 36% | 680 | 42% |
| Diagnosis&Treatment | 12 | 2% | 14 | 4% | 83 | 5% |
| Semiconductors | 6 | 1% | 3 | 1% | 18 | 1% |
| HeatingFood & Medical-Dental | 75 | 12% | 85 | 23% | 266 | 16% |
| Radars | 21 | 3% | 18 | 5% | 83 | 5% |
| Telecommunication Antennas | 43 | 7% | 8 | 2% | 71 | 4% |
| Heating Industrial | 158 | 25% | 107 | 29% | 430 | 26% |

[b]5-year age groups. [a]A total of 16 cases and 11 controls were removed due to missing information on Education. [c]Figures for occupational sections do not add up because many subjects were not assigned to any of the sections and were considered unexposed.

Table 2. Distribution of cumulative RF E-fields and IF H-fields exposure levels based on squared ICNIRP ratio-years (unitless). INTEROCC study. Data from Australia, Canada, France, Germany, Israel, New Zealand, and United Kingdom, 2000-2004.

| **[a]Exposure (metric/window)** | **n** | **Mean(±SD)** | **Minimum** | **25th percentile** | **50th percentile** | **75th percentile** | **90th percentile** | **Maximum** |
|---|---|---|---|---|---|---|---|---|
| **RF E-field cumulative exposure 1-Year Lag** | | | | | | | | |
| Glioma Cases | 224 | 11.61(±50.26) | $3.3*10^{-8}$ | 0.05 | 0.47 | 5.14 | 56.67 | 644.71 |
| Meningioma Cases | 108 | 38.53(±257.54) | $9.9*10^{-13}$ | 0.01 | 0.33 | 4.34 | 50.30 | 2609.03 |
| Controls | 546 | 15.52(±128.58) | $1.1*10^{-15}$ | 0.03 | 0.35 | 2.58 | 53.92 | 2847.03 |
| **RF E-field cumulative exposure 1-4 Years** | | | | | | | | |
| Glioma Cases | 115 | 10.05(±54.43) | $1.3*10^{-5}$ | 0.02 | 0.21 | 2.13 | 22.26 | 507.31 |
| Meningioma Cases | 50 | 3.52(±10.79) | $6.5*10^{-7}$ | 0.02 | 0.31 | 1.86 | 14.71 | 72.01 |
| Controls | 280 | 2.74(±9.98) | $7.6*10^{-10}$ | 0.01 | 0.15 | 1.11 | 13.76 | 104.09 |
| **IF H-field cumulative exposure 1-Year Lag** | | | | | | | | |
| Glioma Cases | 16 | 25.94(±97.37) | 0.01 | 0.07 | 0.25 | 3.26 | 103.21 | 390.96 |
| Meningioma Cases | 9 | 2.34(±3.00) | $9.9*10^{-5}$ | 0.38 | 0.76 | 3.59 | 7.40 | 7.95 |
| Controls | 47 | 22.12(±92.21) | $6.9*10^{-4}$ | 0.07 | 0.68 | 5.37 | 64.28 | 619.02 |
| **IF H-field cumulative Exposure 1-4 Years** | | | | | | | | |
| Glioma Cases | 6 | 1.24(±2.51) | 0.01 | 0.18 | 0.22 | 0.41 | 4.90 | 6.37 |
| Meningioma Cases | 4 | 2.65(±3.74) | $1.5*10^{-5}$ | $4.3*10^{-4}$ | 1.33 | 3.98 | 7.15 | 7.95 |
| Controls | 18 | 3.72(±10.26) | $6.1*10^{-4}$ | 0.08 | 0.26 | 1.40 | 15.55 | 43.48 |

[a]Exposure levels are based on squared ICNIRP ratio-years (arithmetic means).

Table 3. RF and IF sources most frequently reported by the participants and those reported with the highest levels of exposure. INTEROCC study. Data from Australia, Canada, France, Germany, Israel, New Zealand, and United Kingdom, 2000-2004.

| **Most frequent sources** | | | | | | **Sources with highest exposure levels** | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Radiofrequency** | | | **Intermediate frequency** | | | **Radiofrequency** | | | **Intermediate frequency** | | |
| **Source** | **E-field (V/m)** | **N** | **Source** | **H-field (A/m)** | **N** | **Source** | **E-field (V/m)** | **N** | **Source** | **V-field (A/m)** | **N** |
| walkie-talkie | 160 | 411 | induction heater/furnace for metals | 38,6 | 56 | RF sealers/welders for plastic & rubber | 459 | 27 | Electronic Article Surveillance (EAS) systems | 24,5 | 3 |
| microwave heating | 23,4 | 174 | induction heater/furnace for metals | 15 | 56 | TV / VHF / mast / worked on | 310 | 1 | plasma etcher / metal etcher /dry plasma etcher | 4,99 | 15 |
| two-way radio/on motorcycle | 14 | 174 | dielectric heater / plastic & rubber | 333 | 22 | continuous short wave diathermy / physiotherapist | 299 | 12 | induction welding | 3,55 | 4 |
| CB radio | 244 | 153 | glue heater curer / wood & fiber glass | 19 | 16 | shuttle tray machine for plastic & rubber | 264 | 2 | electrical resistance furnaces / metals | 3,1 | 32 |
| RF sealers/welders for plastic & rubber | 459 | 26 | surgical diathermy equipment / surgeon | 12 | 12 | CB radio | 244 | 168 | dielectric heater / plastic & rubber | 1,8 | 28 |
| telecommunication and personal services misc./ground /surrounding | 11,1 | 24 | ultrasound diathermy / physiotherapist | 1,1 | 12 | TV / UHF / mast / worked on | 210 | 8 | metal detectors | 1,27 | 4 |
| dielectric heater / plastic & rubber | 102 | 22 | plasma etcher / metal etcher /dry plasma etcher | 0,17 | 9 | walkie-talkie | 160 | 517 | induction heater/furnace for metals | 0,73 | 60 |
| navigation radar / work sorrounded | 1,23 | 20 | plasma-enhanced chemical vapor deposition (CVD) | 11 | 4 | microwave diathermy / physiotherapist | 106 | 7 | dielectric heater / wood & fiber glass | 0,72 | 1 |
| mobile phone base station antennas /ground / worked on | 0,36 | 16 | induction welding / metal | 42 | 4 | dielectric heater / plastic & rubber | 102 | 28 | glueing press / wood & fiber glass | 0,72 | 6 |
| pulsed short wave diathermy / physiotherapist | 60,1 | 16 | glueing press / wood & fiber glass | 100 | 4 | Radio / FM / mast / worked on | 92 | 1 | induction welding / metal | 0,72 | 4 |

Table 4. Adjusted ORs (95% CIs) for glioma and meningioma for all subjects based on cumulative RF E-field exposures for various exposure lags and windows (1-year, 5-year, and 10-year lags, and time windows 1- to 4-year and 5- to 9-year), before the diagnosis/reference date. INTEROCC study, 2000-2004, from Australia, Canada, France, Germany, Israel, New Zealand and United Kingdom.

| | **Glioma** | | | **Meningioma** | | |
|---|---|---|---|---|---|---|
| **Cumulative exposure (RF E-field, squared ICNIRP ratio-year)**[a] | **Cases** | **Controls** | **OR (95% CIs)** | **Cases** | **Controls** | **OR (95% CIs)** |
| 1-year lag | | | | | | |
| Non exposed | 1,720 | 4,835 | 1.00 (ref.) | 1,745 | 4,828 | 1.00 (ref.) |
| <0.1 | 78 | 194 | 0.85 (0.64-1.13) | 41 | 177 | 0.79 (0.54-1.13) |
| 0.1≥-1.00 | 52 | 146 | 0.65 (0.46-0.90) | 25 | 145 | 0.85 (0.54-1.34) |
| 1.00≥-5.00 | 37 | 101 | 0.71 (0.48-1.05) | 16 | 96 | 0.83 (0.48-1.46) |
| 5.00≥-10.0 | 23 | 21 | 1.83 (1.00-3.39) | 7 | 21 | 1.45 (0.58-3.62) |
| ≥10.0 | 33 | 80 | 0.88 (0.57-1.35) | 19 | 80 | 1.16 (0.68-1.98) |
| 5-year lag | | | | | | |
| Non exposed | 1,720 | 4,835 | 1.00 (ref.) | 1,745 | 4,828 | 1.00 (ref.) |
| <0.1 | 68 | 179 | 0.80 (0.59-1.07) | 37 | 162 | 0.80 (0.54-1.17) |
| 0.1≥-1.00 | 41 | 126 | 0.61 (0.42-0.88) | 22 | 123 | 0.86 (0.53-1.39) |
| 1.00≥-5.00 | 30 | 88 | 0.67 (0.44-1.04) | 16 | 84 | 0.95 (0.54-1.67) |
| ≥5.00 | 49 | 91 | 1.08 (0.75-1.57) | 24 | 91 | 1.30 (0.80-2.10) |
| 10-year lag | | | | | | |
| Non exposed | 1,720 | 4,835 | 1.00 (ref.) | 1,745 | 4,828 | 1.00 (ref.) |
| <0.1 | 60 | 173 | 0.71 (0.52-0.96) | 34 | 158 | 0.80 (0.54-1.19) |
| 0.1≥-1.00 | 28 | 98 | 0.60 (0.39-0.93) | 20 | 94 | 1.02 (0.61-1.71) |
| 1.00≥-5.00 | 24 | 63 | 0.76 (0.46-1.24) | 10 | 62 | 0.87 (0.43-1.74) |
| ≥5.00 | 40 | 82 | 0.98 (0.65-1.46) | 20 | 82 | 1.20 (0.71-2.02) |
| 5-9 years | | | | | | |
| Non exposed | 1,720 | 4,835 | 1.00 (ref.) | 1,745 | 4,828 | 1.00 (ref.) |
| <0.1 | 52 | 117 | 0.89 (0.63-1.25) | 22 | 109 | 0.73 (0.45-1.18) |
| 0.1≥-1.00 | 31 | 71 | 0.84 (0.54-1.31) | 11 | 68 | 0.90 (0.46-1.78) |
| 1.00≥-5.00 | 21 | 47 | 0.83 (0.48-1.42) | 13 | 46 | 1.56 (0.81-3.01) |
| ≥5.00 | 16 | 41 | 0.84 (0.46-1.54) | 8 | 40 | 1.00 (0.45-2.24) |
| 1-4 years | | | | | | |
| Non exposed | 1,720 | 4,835 | 1.00 (ref.) | 1,745 | 4,828 | 1.00 (ref.) |
| <0.1 | 45 | 132 | 0.68 (0.48-0.98) | 20 | 121 | 0.60 (0.36-0.99) |
| 0.1≥-1.00 | 33 | 75 | 0.81 (0.53-1.25) | 13 | 75 | 1.03 (0.55-1.93) |
| 1.00≥-5.00 | 20 | 42 | 0.87 (0.50-1.52) | 11 | 42 | 1.39 (0.68-2.86) |
| ≥5.00 | 16 | 28 | 1.17 (0.62-2.21) | 6 | 28 | 1.02 (0.40-2.57) |

[a] Adjusted ORs calculated using conditional logistic regression with a strata variable including 5-year age group, sex, country, and region, and adjusted by education. [a]Exposure groups based on fixed cut points depending on the cumulative exposure distribution of controls. Confidence intervals based on Wald test.

Table 5. Adjusted ORs for glioma using continuous RF E-field exposures (1-year lag and 1- to 4-year window) and various polynomial models for all subjects and only males. INTEROCC study, 2000-2004, from Australia, Canada, France, Germany, Israel, New Zealand and United Kingdom.

| Model # | Model form | Odds Ratio | 95%CI[a] | AIC | BIC |
|---|---|---|---|---|---|
| **RF E-field cumulative exposure overall 1-year lag (all subjects)** | | | | | |
| 1 | Log-linear | 1.00 | 0.99-1.00 | 6711.97 | 6728.54 |
| 2 | Log-log | 1.03 | 0.91-1.16 | 6711.84 | 6728.41 |
| 3 | Log-quadratic | 1.00 (linear term) | 0.99-1.00 | 6713.32 | 6735.42 |
| | | 1.00 (quadratic term) | 1.00-1.00 | | |
| 4 | Translog-quadratic | 1.01 (linear term) | 0.74-1.37 | 6713.82 | 6735.92 |
| | | 1.01 (quadratic term) | 0.94-10.7 | | |
| **RF E-field cumulative exposure 1- to 4-year exposure window (all subjects)** | | | | | |
| 1 | Log-linear | 1.01 | 1.00-1.02 | 6730.19 | 6750.74 |
| 2 | Log-log | 1.06 | 0.88-1.28 | 6734.54 | 6755.08 |
| 3 | Log-quadratic | 1.00 (linear term) | 0.87-1.03 | 6731.57 | 6758.96 |
| | | 1.00 (quadratic term) | 0.99-1.00 | | |
| 4 | Translog-quadratic | 0.66 (linear term) | 0.43-1.09 | 6731.95 | 6759.33 |
| | | 1.15 (quadratic term) | 1.01-1.30 | | |
| **RF E-field cumulative exposure overall 1-year lag (male subjects only)** | | | | | |
| 1 | Log-linear | 1.00 | 1.00-1.00 | 3864.65 | 3879.83 |
| 2 | Log-log | 0.97 | 0.87-1.08 | 3865.77 | 3880.94 |
| 3 | Log-quadratic | 1.00 (linear term) | 1.00-1.00 | 7159.80 | 7182.08 |
| | | 1.00 (quadratic term) | 1.00-1.00 | | |
| 4 | Translog-quadratic | 0.94 (linear term) | 0.73-1.22 | 7160.37 | 7182.66 |
| | | 1.00 (quadratic term) | 0.95-1.07 | | |
| **RF E-field cumulative exposure 1- to 4-year exposure window (male subjects only)** | | | | | |
| 1 | Log-linear | 1.01 | 0.99-1.03 | 3864.46 | 3879.63 |
| 2 | Log-log | 1.03 | 0.83-1.27 | 3865.95 | 3881.13 |
| 3 | Log-quadratic | 0.99 (linear term) | 0.97-1.02 | 7155.13 | 7177.42 |
| | | 1.00 (quadratic term) | 1.00-1.00 | | |
| 4 | Translog-quadratic | 0.68 (linear term) | 0.43-1.08 | 7155.61 | 7177.90 |
| | | 1.15 (quadratic term) | 1.01-1.30 | | |

[a] Confidence intervals (CI) based on profile log-likelihood.

Table 6. Adjusted ORs for meningioma using continuous RF E-field exposures (1-year lag and 1- to 4-year window) and various polynomial models for all subjects and only males. INTEROCC study, 2000-2004, from Australia, Canada, France, Germany, Israel, New Zealand and United Kingdom.

| Model # | Model form | Odds Ratio | 95%CI[a] | AIC | BIC |
|---|---|---|---|---|---|
| **RF E-field cumulative exposure overall 1-year lag (all subjects)** | | | | | |
| 1 | Log-linear | 1.00 | 1.00-1.00 | 6711.96 | 6728.54 |
| 2 | Log-log | 1.03 | 0.91-1.16 | 6711.84 | 6728.41 |
| 3 | Log-quadratic | 1.00 (linear term) | 1.00-1.00 | 6713.32 | 6735.42 |
| | | 1.00 (quadratic term) | 1.00-1.00 | | |
| 4 | Translog-quadratic | 1.01 (linear term) | 0.74-1.37 | 6713.81 | 6735.91 |
| | | 1.01 (quadratic term) | 0.94-1.07 | | |
| **RF E-field cumulative exposure 1- to 4-year exposure window (all subjects)** | | | | | |
| 1 | Log-linear | 1.00 | 0.97-1.03 | 6712.03 | 6728.60 |
| 2 | Log-log | 1.06 | 0.82-1.39 | 6711.83 | 6728.40 |
| 3 | Log-quadratic | 1.03 (linear term) | 0.96-1.10 | 6713.39 | 6735.49 |
| | | 1.00 (quadratic term) | 1.00-1.00 | | |
| 4 | Translog-quadratic | 1.28 (linear term) | 0.54-2.67 | 6713.50 | 6735.60 |
| | | 0.94 (quadratic term) | 0.75-1.17 | | |
| **RF E-field cumulative exposure overall 1-year lag (male subjects only)** | | | | | |
| 1 | Log-linear | 0.99 | 0.99-1.00 | 1992.01 | 2004.54 |
| 2 | Log-log | 1.04 | 0.89-1.21 | 1992.06 | 2004.59 |
| 3 | Log-quadratic | 1.00 (linear term) | 0.99-1.01 | 6713.32 | 6735.42 |
| | | 1.00 (quadratic term) | 1.00-1.00 | | |
| 4 | Translog-quadratic | 1.01 (linear term) | 0.74-1.37 | 6713.82 | 6735.92 |
| | | 1.01 (quadratic term) | 0.94-1.07 | | |
| **RF E-field cumulative exposure 1- to 4-year exposure window (male subjects only)** | | | | | |
| 1 | Log-linear | 1.03 | 1.00-1.06 | 1990.12 | 2002.65 |
| 2 | Log-log | 1.25 | 0.92-1.71 | 1990.50 | 2003.03 |
| 3 | Log-quadratic | 1.03 (linear term) | 0.95-1.10 | 6713.39 | 6735.49 |
| | | 1.00 (quadratic term) | 0.99-1.00 | | |
| 4 | Translog-quadratic | 1.28 (linear term) | 0.64-2.56 | 6713.50 | 6735.60 |
| | | 0.94 (quadratic term) | 0.74-1.17 | | |

[a] Confidence intervals (CI) based on profile log-likelihood.

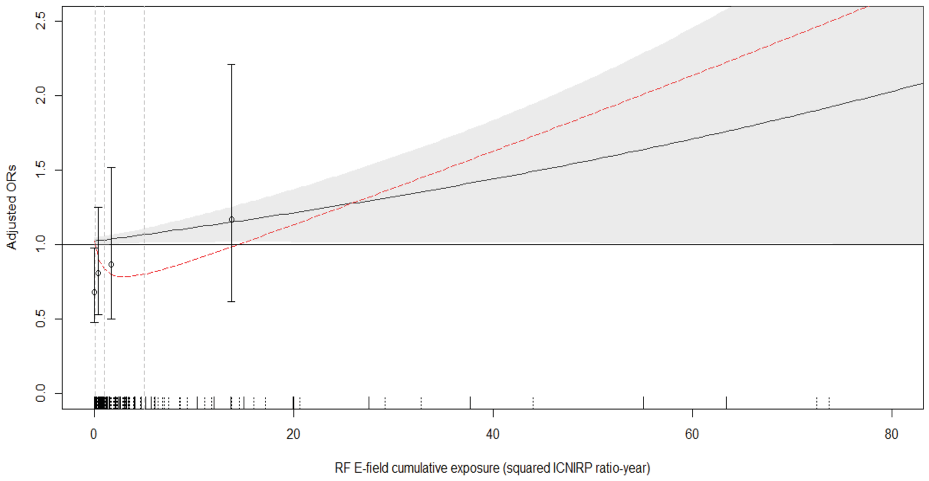


Figure 2. Exposure-response association between risk of glioma (adjusted Odds Ratios) and RF E-field cumulative exposure (1- to 4-year lag), based on squared ICNIRP ratio-years, using a linear model (continuous black line) and a quadratic model with log-transformed exposure (dashed red line). Plot rug are cases (continuous lines) and controls (dashed lines). The grey shadow indicates 95% CIs for the linear model based on the profile likelihood. Vertical dashed lines indicate fixed cut points for the cumulative exposure distribution (i.e. <0.1; 0.1-1; 1-5; ≥5). Points and error bars indicate adjusted ORs and 95% CI for the exposure categories based on these cut points. The points are positioned at the median exposure for each interval. Plot truncated at the 99th percentile of cumulative exposure.

Table 7. Adjusted ORs (95% CIs) for glioma and meningioma for all subjects based on cumulative IF H-field exposures for various exposure lags and windows (1-year, 5-year, and 10-year lags, and time windows 1- to 4-year and 5- to 9-year), before the diagnosis/reference date. INTEROCC study, 2000-2004, from Australia, Canada, France, Germany, Israel, New Zealand and United Kingdom.

| | **Glioma** | | | **Meningioma** | | |
|---|---|---|---|---|---|---|
| **Cumulative exposure (IF H-field squared ICNIRP ratio, unitless)**[a] | **Cases** | **Controls** | **OR (95% CIs)** | **Cases** | **Controls** | **OR (95% CIs)** |
| 1-year lag | | | | | | |
| Non exposed | 3,973 | 10,904 | 1.00 (ref.) | 3,701 | 10,638 | 1.00 (ref.) |
| <0.11 | 15 | 38 | 0.72 (0.39-1.34) | 5 | 34 | 0.69 (0.26-1.84) |
| ≥0.11 | 9 | 38 | 0.56 (0.27-1.18) | 7 | 33 | 0.98 (0.42-2.31) |
| 5-year lag | | | | | | |
| Non exposed | 3,973 | 10,904 | 1.00 (ref.) | 3,701 | 10,638 | 1.00 (ref.) |
| <0.09 | 13 | 38 | 0.63 (0.33-1.21) | 6 | 34 | 0.82 (0.33-2.03) |
| ≥0.09 | 11 | 38 | 0.67 (0.33-1.33) | 6 | 33 | 0.85 (0.34-2.11) |
| 10-year lag | | | | | | |
| Non exposed | 3,973 | 10,904 | 1.00 (ref.) | 3,701 | 10,638 | 1.00 (ref.) |
| <0.08 | 17 | 44 | 0.77 (0.43-1.37) | 7 | 39 | 0.87 (0.37-2.02) |
| ≥0.08 | 7 | 32 | 0.47 (0.20-1.09) | 5 | 28 | 0.79 (0.29-2.13) |
| 5-9 years | | | | | | |
| Non exposed | 3,973 | 10,904 | 1.00 (ref.) | 3,701 | 10,638 | 1.00 (ref.) |
| <0.04 | 15 | 138 | 0.52 (0.29-1.94) | 11 | 49 | 1.07 (0.53- 2.12) |
| ≥0.04 | 9 | 69 | 1.04 (0.46-2.33) | 1 | 18 | 0.24 (0.03-1.88) |
| 1-4 years | | | | | | |
| Non exposed | 3,973 | 10,904 | 1.00 (ref.) | 3,701 | 10,638 | 1.00 (ref.) |
| <0.03 | 17 | 60 | 0.54 (0.31-0.94) | 10 | 54 | 0.86 (0.43-1.75) |
| ≥0.03 | 7 | 16 | 1.19 (0.47-2.98) | 2 | 13 | 0.72 (0.15-3.44) |

[a]Adjusted ORs calculated using conditional logistic regression with a strata variable including 5-year age group, sex, country, and region, and adjusted by education. [a]Cut points based on the median or 50th percentile of the cumulative exposure distribution of controls. Confidence intervals based on Wald test.

Table 8. Adjusted ORs (95% CIs) for glioma and meningioma for male subjects based on cumulative RF E-field exposures for various exposure lags and windows (1-year, 5-year, and 10-year lags, and time windows 1- to 4-year and 5- to 9-year), before the diagnosis/reference date. INTEROCC study, 2000-2004, from Australia, Canada, France, Germany, Israel, New Zealand and United Kingdom.

| | **Glioma** | | | **Meningioma** | | |
|---|---|---|---|---|---|---|
| **Cumulative exposure (RF E-field, squared ICNIRP ratio-year)[a]** | **Cases** | **Controls** | **OR (95% CIs)** | **Cases** | **Controls** | **OR (95% CIs)** |
| 1-year lag | | | | | | |
| Non exposed | 978 | 1,943 | 1.00 (ref.) | 420 | 1,937 | 1.00 (ref.) |
| <0.1 | 58 | 127 | 0.84 (0.60-1.16) | 18 | 114 | 0.70 (0.41-1.20) |
| 0.1≥-1.00 | 44 | 114 | 0.63 (0.44-0.91) | 15 | 112 | 0.81 (0.45-1.45) |
| 1.00≥-5.00 | 32 | 79 | 0.69 (0.45-1.07) | 11 | 74 | 0.95 (0.48-1.85) |
| 5.00≥-10.0 | 22 | 20 | 1.83 (0.97-3.43) | 4 | 20 | 0.97 (0.32-2.98) |
| ≥10.0 | 29 | 64 | 0.84 (0.53-1.33) | 13 | 64 | 1.28 (0.68-2.43) |
| 5-year lag | | | | | | |
| Non exposed | 978 | 1,943 | 1.00 (ref.) | 420 | 1,937 | 1.00 (ref.) |
| <0.1 | 51 | 124 | 0.75 (0.53-1.07) | 17 | 110 | 0.72 (0.42-1.25) |
| 0.1≥-1.00 | 35 | 96 | 0.61 (0.41-0.92) | 14 | 94 | 0.90 (0.50-1.65) |
| 1.00≥-5.00 | 28 | 68 | 0.73 (0.46-1.16) | 11 | 64 | 1.05 (0.53-2.08) |
| ≥5.00 | 45 | 76 | 1.06 (0.72-1.57) | 16 | 76 | 1.29 (0.72-2.30) |
| 10-year lag | | | | | | |
| Non exposed | 978 | 1,943 | 1.00 (ref.) | 420 | 1,937 | 1.00 (ref.) |
| <0.1 | 50 | 123 | 0.74 (0.52-1.04) | 18 | 111 | 0.77 (0.45-1.32) |
| 0.1≥-1.00 | 22 | 78 | 0.55 (0.34-0.89) | 15 | 74 | 1.17 (0.64-2.12) |
| 1.00≥-5.00 | 23 | 47 | 0.86 (0.51-1.45) | 6 | 46 | 0.95 (0.39-2.29) |
| ≥5.00 | 37 | 71 | 0.97 (0.63-1.47) | 14 | 71 | 1.20 (0.65-2.21) |
| 5-9 years | | | | | | |
| Non exposed | 978 | 1,943 | 1.00 (ref.) | 420 | 1,937 | 1.00 (ref.) |
| <0.1 | 39 | 77 | 0.87 (0.58-1.30) | 7 | 70 | 0.50 (0.22-1.12) |
| 0.1≥-1.00 | 29 | 59 | 0.89 (0.56-1.43) | 8 | 57 | 0.91 (0.41-2.01) |
| 1.00≥-5.00 | 19 | 43 | 0.77 (0.44-1.36) | 9 | 42 | 1.26 (0.58-2.71) |
| ≥5.00 | 15 | 30 | 0.91 (0.48-1.74) | 6 | 29 | 1.54 (0.60-3.91) |
| 1-4 years | | | | | | |
| Non exposed | 978 | 1,943 | 1.00 (ref.) | 420 | 1,937 | 1.00 (ref.) |
| <0.1 | 35 | 84 | 0.70 (0.46-1.06) | 8 | 77 | 0.48 (0.22-1.03) |
| 0.1≥-1.00 | 28 | 66 | 0.74 (0.46-1.17) | 7 | 65 | 0.69 (0.30-1.58) |
| 1.00≥-5.00 | 17 | 39 | 0.77 (0.42-1.39) | 6 | 37 | 1.10 (0.44-2.74) |
| ≥5.00 | 14 | 20 | 1.20 (0.59-2.42) | 6 | 20 | 2.02 (0.75-5.39) |

[a]Adjusted ORs calculated using conditional logistic regression with a strata variable including 5-year age group, sex, country, and region, and adjusted by education. [a]Exposure groups based on fixed cut points depending on the cumulative exposure distribution of controls. Confidence intervals based on Wald test.

## ACKNOWLEDGEMENTS

The authors would like to give special thanks to Dr. Dave Conover (deceased), USA, for his contribution in the assignment of RF and IF EMF sources to study subjects, as well as to Taichi Murata, Japan, for his work on exposure models for military radars and antennas.

## DISCLAIMER

The findings and conclusions in this paper have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.

## REFERENCES

1 Deltour I, Johansen C, Auvinen A, Feychting M, Klaeboe L, Schüz J. Time Trends in Brain Tumor Incidence Rates in Denmark, Finland, Norway, and Sweden, 1974–2003. *J Natl Cancer Inst* 2009; **101**: 1721–1724.

2 Hardell L, Carlberg M, Söderqvist F, Mild KH. Re: Time trends in brain tumor incidence rates in Denmark, Finland, Norway, and Sweden, 1974-2003. *J Natl Cancer Inst* 2010; **102**: 740-741-743.

3 Ostrom QT, Gittleman H, Fulop J, Liu M, Blanda R, Kromer C *et al.* CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2008-2012. *Neuro-Oncol* 2015; **17 Suppl 4**: iv1-iv62.

4 Arora RS, Alston RD, Eden TOB, Estlin EJ, Moran A, Geraci M *et al.* Are reported increases in incidence of primary CNS tumours real? An analysis of longitudinal trends in England, 1979-2003. *Eur J Cancer Oxf Engl 1990* 2010; **46**: 1607–1616.

5 Bondy ML, Scheurer ME, Malmer B, Barnholtz-Sloan JS, Davis FG, Il'yasova D *et al.* Brain tumor epidemiology: consensus from the Brain Tumor Epidemiology Consortium. *Cancer* 2008; **113**: 1953–1968.

6 Fisher JL, Schwartzbaum JA, Wrensch M, Wiemels JL. Epidemiology of brain tumors. *Neurol Clin* 2007; **25**: 867–890, vii.

7 Lönn S, Klaeboe L, Hall P, Mathiesen T, Auvinen A, Christensen HC *et al.* Incidence trends of adult primary intracerebral tumors in four Nordic countries. *Int J Cancer* 2004; **108**: 450–455.

8 Wiemels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. *J Neurooncol* 2010; **99**: 307–314.

9 Schwartzbaum JA, Fisher JL, Aldape KD, Wrensch M. Epidemiology and molecular pathology of glioma. *Nat Clin Pract Neurol* 2006; **2**: 494–503; quiz 1 p following 516.

10 Braganza MZ, Kitahara CM, Berrington de Gonzalez A, Inskip PD, Johnson KJ, Rajaraman P. Ionizing radiation and the risk of brain and central nervous system tumors: a systematic review. *Neuro-Oncol* 2012; **14**: 1316–1324.

11 Connelly JM, Malkin MG. Environmental risk factors for brain tumors. *Curr Neurol Neurosci Rep* 2007; **7**: 208–214.

12 Ohgaki H. Epidemiology of brain tumors. *Methods Mol Biol Clifton NJ* 2009; **472**: 323–342.

13 IARC. Non-ionizing radiation, Part 2: Radiofrequency electromagnetic fields. *Int Agency Res Cancer Work Group Eval Carcinog Risks Hum* 2013; **102**: 1–460.

14 Lilienfeld A. *Foreign service health status study: evaluation of health status of foreign service and other employees from selected Eastern European posts : final report*. Dept. of Epidemiology, School of Hygiene and Public Health, Johns Hopkins University: Baltimore, Md, 1978https://catalyst.library.jhu.edu/catalog/bib_1807.

15 Tynes T, Hannevik M, Andersen A, Vistnes A, Haldorsen T. Incidence of breast cancer in Norwegian female radio and telegraph operators. *Cancer Causes Control* 1996; **7**: 197–204.

16 Lagorio S, Rossi S, Vecchia P, De Santis M, Bastianini L, Fusilli M *et al.* Mortality of plastic-ware workers exposed to radiofrequencies. *Bioelectromagnetics* 1997; **18**: 418–421.

17 Morgan RW, Kelsh MA, Zhao K, Exuzides KA, Heringer S, Negrete W. Radiofrequency exposure and mortality from cancer of the brain and lymphatic/hematopoietic systems. *Epidemiol Camb Mass* 2000; **11**: 118–127.

18 Robinette CD, Silverman C, Jablon S. Effects upon health of occupational exposure to microwave radiation (radar). *Am J Epidemiol* 1980; **112**: 39–53.

19 Szmigielski S. Cancer morbidity in subjects occupationally exposed to high frequency (radiofrequency and microwave) electromagnetic radiation. *Sci Total Environ* 1996; **180**: 9–17.

20 Sienkiewicz Z, Schüz J, Cardis E. Risk analysis of human exposure to electromagnetic fields (revised). Deliverable Report D2 of EHFRAN project. 2010.http://efhran.polimi.it/docs/EFHRAN_D2_final.pdf.

21 SCENIHR. Health Effects of Exposure to EMF. Scientific Committee on Emerging and Newly Identified Health Risks. 2009.http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_022.pdf.

22 Deltour I, Wiart J, Taki M, Wake K, Varsier N, Mann S *et al.* Analysis of three-dimensional SAR distributions emitted by mobile phones in an epidemiological perspective. *Bioelectromagnetics* 2011; **32**: 634–643.

23 Cardis E, Armstrong BK, Bowman JD, Giles GG, Hours M, Krewski D *et al.* Risk of brain tumours in relation to estimated RF dose from mobile phones: results from five Interphone countries. *Occup Environ Med* 2011; **68**: 631–640.

24 Berg G, Spallek J, Schüz J, Schlehofer B, Böhler E, Schlaefer K *et al.* Occupational exposure to radio frequency/microwave radiation and the risk of brain tumors: Interphone Study Group, Germany. *Am J Epidemiol* 2006; **164**: 538–548.

25 Karipidis KK, Benke G, Sim MR, Kauppinen T, Giles G. Occupational exposure to ionizing and non-ionizing radiation and risk of glioma. *Occup Med Oxf Engl* 2007; **57**: 518–524.

26 Groves FD, Page WF, Gridley G, Lisimaque L, Stewart PA, Tarone RE *et al.* Cancer in Korean war navy technicians: mortality survey after 40 years. *Am J Epidemiol* 2002; **155**: 810–818.

27 ICNIRP. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). International Commission on Non-Ionizing Radiation Protection. *Health Phys* 1998; **74**: 494–522.

28 Barnes FS, Greenebaum B. The effects of weak magnetic fields on radical pairs. *Bioelectromagnetics* 2015; **36**: 45–54.

29 Pall ML. Electromagnetic fields act via activation of voltage-gated calcium channels to produce beneficial or adverse effects. *J Cell Mol Med* 2013; **17**: 958–965.

30 Wyde M, Cesta M, Blystone C, Elmore S, Foster P, Hooth M *et al.* Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposure). *bioRxiv* 2016. doi:10.1101/055699.

31 Lai H, Singh NP. Acute low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells. *Bioelectromagnetics* 1995; **16**: 207–210.

32 Paulraj R, Behari J. Single strand DNA breaks in rat brain cells exposed to microwave radiation. *Mutat Res* 2006; **596**: 76–80.

33 Ahlbom A, Bridges J, de Seze R, Hillert L, Juutilainen J, Mattsson M-O *et al.* Possible effects of electromagnetic fields (EMF) on human health--opinion of the scientific committee on emerging and newly identified health risks (SCENIHR). *Toxicology* 2008; **246**: 248–250.

34 Repacholi MH. Low-level exposure to radiofrequency electromagnetic fields: health effects and research needs. *Bioelectromagnetics* 1998; **19**: 1–19.

35 Poulletier de Gannes F, Lagroye I, Veyret B. D3 - Report on the analysis of risks associated to exposure to EMF:in vitro and in vivo (animals) studies. 2010.http://efhran.polimi.it/ docs/IMS-EFHRAN_09072010.pdf (accessed 16 Aug2016).

36 Lerchl A, Klose M, Grote K, Wilhelm AFX, Spathmann O, Fiedler T *et al.* Tumor promotion by exposure to radiofrequency electromagnetic fields below exposure limits for humans. *Biochem Biophys Res Commun* 2015; **459**: 585–590.

37 Vila J, Bowman JD, Richardson L, Kincl L, Conover DL, McLean D *et al.* A Source-based Measurement Database for Occupational Exposure Assessment of Electromagnetic Fields in the INTEROCC Study: A Literature Review Approach. *Ann Occup Hyg* 2016; **60**: 184–204.

38 Vila J, Bowman JD, Figuerola J, Morina D, Kincl L, Richardson L *et al.* Development of a source-exposure matrix for occupational exposure assessment of electromagnetic fields in the INTEROCC study. *J Expo Sci Env Epidemiol* 2016; **In press**.

39 Cardis E, Richardson L, Deltour I, Armstrong B, Feychting M, Johansen C *et al.* The INTERPHONE study: design, epidemiological methods, and description of the study population. *Eur J Epidemiol* 2007; **22**: 647–664.

40 ICNIRP. Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz-300 GHz) - Review of the Scientific Evidence and Health Consequences. 2009.http://www.icnirp.org/en/publications/article/hf-review-2009.html (accessed 16 Sep2016).

41 Röösli M, Vienneau D. Epidemiological Exposure Assessment. In: *Epidemiology of Electromagnetic Fields*. CRC Press, 2014, p 368.

42 Vrieze SI. Model selection and psychological theory: a discussion of the differences between the Akaike information criterion (AIC) and the Bayesian information criterion (BIC). *Psychol Methods* 2012; **17**: 228–243.

43 R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/. 2014.

44 Therneau T. A Package for Survival Analysis in S. version 2.38, http://CRAN.R-project.org/package=survival. 2015.

45 StataCorp. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. 2015.

46 Milham S. Mortality by license class in amateur radio operators. *Am J Epidemiol* 1988; **128**: 1175–1176.

47 Finkelstein MM. Cancer incidence among Ontario police officers. *Am J Ind Med* 1998; **34**: 157–162.

48 Grayson JK. Radiation exposure, socioeconomic status, and brain tumor risk in the US air force: a nested case-control study. *Am J Epidemiol* 1996; **143**: 480–486.

49 Thomas TL, Stolley PD, Stemhagen A, Fontham ET, Bleecker ML, Stewart PA *et al.* Brain tumor mortality risk among men with electrical and electronics jobs: a case-control study. *J Natl Cancer Inst* 1987; **79**: 233–238.

50 Cardis E. Deliverable D17: Report on health effects of RF with recommendations for non-ionising radiation protection and research needs. 2009.https://www.emf-portal.org/en/article/20058.

51 Turner MC, Benke G, Bowman JD, Figuerola J, Fleming S, Hours M *et al.* Occupational exposure to extremely low frequency magnetic fields and brain tumour risks in the INTEROCC study. *Cancer Epidemiol Biomarkers Prev* 2014. doi:10.1158/1055-9965.EPI-14-0102.

52 SCENIHR. Possible Effects of Electromagnetic Fields (EMF) on Human Health. European Commission: Health and Consumer Protection; Directorate General: Brussles, 2007.

53 Joseph W, Vermeeren G, Verloock L, Goeminne F. In situ magnetic field exposure and ICNIRP-based safety distances for electronic article surveillance systems. *Radiat Prot Dosimetry* 2012; **148**: 420–427.

54 ICNIRP. ICNIRP statement related to the use of security and similar devices utilizing electromagnetic fields. *Health Phys* 2004; **87**: 187–196.

55 Royston P, Sauerbrei W, Altman DG. Modeling the effects of continuous risk factors. *J Clin Epidemiol* 2000; **53**: 219–221.

56 Hastie T, Tibshirani R, Friedman J. *The Elements of Statistical Learning: Data Mining, Inference, and Prediction*. Springer: New York, 2001.

57 Peng L. Empirical-Likelihood-Based Confidence Interval for the Mean with a Heavy-Tailed Distribution. *Ann Stat* 2004; **32**: 1192–1214.

58 Murphy SA. Likelihood Ratio-Based Confidence Intervals in Survival Analysis. *J Am Stat Assoc* 1995; **90**: 1399–1405.

59 Ahlbom A, Green A, Kheifets L, Savitz D, Swerdlow A. Epidemiology of Health Effects of Radiofrequency Exposure. *Environ Health Perspect* 2004; **112**: 1741–1754.

60 Röösli M. *Epidemiology of Electromagnetic Fields*. CRC Press, 2014http://www.crcpress.com/product/isbn/9781466568167.

61 Kriebel D, Checkoway H, Pearce N. Exposure and dose modelling in occupational epidemiology. *Occup Environ Med* 2007; **64**: 492–498.

62 Lin J. *Electromagnetic Fields in Biological Systems*. CRC Press, 2011.

63 Baste V, Mild KH, Moen BE. Radiofrequency exposure on fast patrol boats in the Royal Norwegian Navy—an approach to a dose assessment. *Bioelectromagnetics* 2010; **31**: 350–360.

# 5. DISCUSSION

Epidemiological EMF studies based on the use of JEMs may lack power and provide biased estimates of risk due to exposure misclassification which arise from the existence of between-worker variability; since workers with the same job title can be exposed at very different levels. The source-based approach developed in INTEROCC and described in this thesis may reduce this problem, increasing the accuracy of both assigned indices of exposure to study subjects and risk estimates calculated.

In the first paper, we described the methods followed to construct an EMF occupational exposure measurement database (OEMD) from measurements extracted from the literature, supplemented with some expert judgment estimates for EMF sources without available measurements. Literature reviews have become a vital tool in epidemiology, increasing the ability to draw stronger conclusions based on the results obtained from multiple studies (Egger M, 2001; Light and Pillemer, 1984). Similarly, while performing measurements would be time consuming and expensive, retrieving exposure data from the literature allows obtaining measurements for different situations, and covering multiple exposure scenarios. In particular for EMF, exposure data extracted from the literature has traditionally been used to construct job-exposure matrices or reconstruct past exposures using modelling and regression techniques (Bowman et al., 2007; Koh et al., 2015; Lavoué et al., 2007).

In this article, we showed that exposure data can be obtained not only from published resources, such as peer-reviewed articles, but also from published and unpublished technical reports. This sometimes hard to obtain source of information, sometimes referred to as “grey literature”, has proved to be tremendously useful in obtaining measurements for rare or less common sources of exposure, and other information not usually found in the published literature (Auger, 1998). In our study, over 30% of the data collected in the OEMD was obtained using this type of resources.

The availability of exposure measurements for specific sources of EMF exposure in the workplace fills a gap highlighted by several authors (Kheifets et al., 2009; Stam, 2014). These data can also assist occupational hygienists in the implementation of EMF guidelines and regulations in place, by identifying potential sources of exposure and even performing a preliminary workplace assessment of possible exceedances of exposure limit values or action levels established by international organizations (ICNIRP, 2010, 1998b) or through their transposition into national or transnational legislation (European Parliament and Council, 2013). This tool may become particularly useful when workers are exposed to multiple EMF sources, either simultaneously or sequentially. Furthermore, since the OEMD contains measurements for the same sources in their different frequency components, this can also be of use when performing calculations of total exposures, following ICNIRP´s summation methods or others. In some cases, the availability of ancillary information, such as horizontal and vertical distance to the source, anatomical location, duty cycle, measures of dispersion and/or sample size may allow more accurate assessments and calculations of both average exposure levels and their uncertainty.

However, limitations of the OEMD will make difficult or even impossible to use this database for these purposes for some sources, especially those for which only maximum values were retrieved from the literature, when there is low availability of measurements or lack of information on ancillary data. In these cases, the use of the SEM estimates may be a solution to these problems.

Measurement data extraction from the papers/reports was carried out by experts individually, which may have led to errors while copying the information into the database or during conversion of units when necessary. In order to improve the accuracy of this process automated and manual revisions of all the measurements recorded in the OEMD were carried out by the author. Moreover, the addition of the sources of information used allows the identification of unreliable data and their correction if necessary. Measurements also have their own limitations (e.g. systematic errors, lack of duty cycle factor correction etc.). Measurements extracted from the literature have been obtained for different purposes, and using a wide range of instruments and techniques, which adds to the classical errors associated with exposure assessment. In order to reduce these errors, only the measurements that were judged useful for the purpose of this study through the confidence evaluation were selected to be introduced in the measurement database.

Confidence evaluation ratings obtained from EMF experts were used both to include or exclude measurements into the OEMD and later to adjust the exposure estimates in the SEM, in relation to their quality and relevance for use in epidemiological studies, in particular in INTEROCC. Although for many of the selected measurements, this assessment was performed by two experts or more, depending on their availability, followed by discussion to arrive at a consensus evaluation, for some records only one rating was available which may have affected the final estimates. Measurements extracted from review articles were assigned a rating value of 1, due to the lack of the required information to perform a full assessment. Moreover, only measurements that complied with the confidence requirements established in our study (see OEMD paper) were selected and recorded in the database, which may have contributed to the small number of measurements for some EMF sources, increasing the uncertainty of the exposure estimates calculated for them.

Confidence evaluations used in the current version of the SEM were aimed at assessing representativeness for head exposure. Although initially, the development of distance models had been planned within the project, time constraints did not allow the inclusion of these models in this thesis or their use to modify the estimates in the SEM. Therefore, although some efforts were made to develop these models, future efforts will still be needed to adapt the work for application to other organs Although it will not be possible at present to apply these models in studies of outcomes related to organs different than the brain, future versions of the SEM, including these modifications, may allow its use in studies interested in other organs.

Expert elicitation for a group of RF sources without available measurements in the literature had been performed previous to the beginning of this thesis. Although further elicitations were initially planned, it was finally decided to use only measurement data to assign exposures. For this purpose, some measurements were performed by experts from the GERoNiMO project (http://www.crealradiation.com/index.php/en/geronimo-home). For some sources for which no measurements were finally identified or measurement surveys are still pending, analogous sources with similar size, power and frequency were used to assign exposures. Since this only happened with a small number of sources, we expect that the impact on the exposure and risk estimates is small.

For the construction of the SEM, we developed a novel methodology to summarize the exposure data extracted from the literature and collected in the OEMD. These data are usually not reported homogeneously and different statistics might be available depending on the EMF source and the study the data was extracted from. Therefore, our aim was to homogenize the available data in the OEMD in order to construct a source-exposure matrix with mean estimates of exposure (AM and GM) by source and their corresponding estimates of variability (SD and GSD). Because the mean estimates in the SEM were developed for their use in an epidemiological study, INTEROCC, they were aimed at head exposure through the use of the confidence evaluation ratings previously developed as weights during the pooling. As discussed in the paper, this methodology to adjust exposure estimates represents an alternative to the more traditional approaches, commonly based on the use of sample size or inverse variance (Tielemans et al., 2002). Unlike those methods, which adjust the estimates by the variability/uncertainty on the measurements used for the pooling, the use of expert ratings as weights not only takes this into account but also allows the inclusion of other factors in the assessment of quality and relevance of the measurements being pooled (e.g. type of sampling, quality of the instruments and calibration).

The systematic collection, assessment and combination of exposure data from the literature in to a SEM or other forms of database appears as a novel methodology, similar to meta-analysis in epidemiology, which allows taking advantage of past efforts to collect measurements in the workplace or other settings. Although some authors already used similar methods in the past (Koh et al., 2015; Lavoué et al., 2007), "exposure meta-analysis" appears still to be an undeveloped methodology. A Google® Scholar search performed on 11/09/2016 provided 118 hits, most of them unrelated to the field. In this regard, a manuscript is in preparation by the author (Vila, 2016), describing the basic characteristics of this new methodology.

"Exposure meta-analyses" have been mostly performed with the purpose of exposure modelling or meta-regression, where exposure statistics for a specific agent are combined with exposure determinants using commonly linear regression in order to determine which determinants drive the exposure to a bigger extent and therefore lead better control measures. Many of these "meta-analysis" efforts highlighted the fact that exposure data had to be discarded if appropriate summary statistics were not provided in the studies. Therefore, the authors mostly kept only those values which could be readily used for the pooling, excluding those which could not be used directly. However, the SEM methodology allowed for the use of exposure data which other methods may have discarded.

While for the first objective of the thesis, we covered all EMF frequency bands (0 Hz – 300 GHz) through the development of the OEMD and the SEM databases, objectives two and three focused on exposures from IF and RF sources. The development of individual indices of exposure and their use in the analysis of brain tumours risk associated with exposures to ELF sources will also be performed shortly, which will lead to further publications. Although the assessment of exposure to static magnetic fields was not initially planned, the availability of the measurements collected and the exposure estimates obtained from them will allow their future use in this or other studies.

The results for ICNIRP ratios for both RF and IF EMF sources showed that reference levels were exceeded various orders of magnitude in at least one fourth of all sources. Around 10% of subjects were considered exposed to at least one source per job, of the 35,800 jobs reported in INTEROCC, including sources in all sections, particularly radar, broadcasting, telecommunications, semiconductor manufacturing, medical diagnosis and treatment, industrial heating, and food preparation. Results for cumulative exposures gave an interquartile range ratio around 90, which is sufficient to detect an exposure-response association, if one exists.

Our third paper presents the results of the largest case-control study to date on occupational exposure to RF or IF EMF and brain tumours risk, with almost 2,000 cases of glioma and a similar number for meningioma, as well as over 5,000 controls. The availability of this large population allowed the assessment of cumulative exposures both overall and in different time windows, an approach only possible in a large study like this. The use of the novel exposure assessment methods developed within the project allowed the assignment of individual exposure estimates, taking into account the special characteristics of the work performed by each study subject in relation to the use or proximity to RF and/or IF EMF sources.

Overall, the results of the risk analyses gave few positive associations for both glioma and meningioma and cumulative exposures to RF or IF EMF. However, some positive associations were seen for both agents and the highest exposed groups in the exposure time windows closer to the diagnosis/reference date, for glioma, and in all time windows for meningioma. These results highlight the difficulties of identifying risks from high frequency EMF exposures even in a large population since, at it was the case in our study, most subjects were not exposed, which reduced the power to identify stronger associations, if they exist.

Our findings are in agreement with past studies where quantitative exposure data were used (Lagorio et al., 1997; Szmigielski, 1996; Tynes et al., 1996). However, most of these studies considered exposures to sources in the RF band as a whole, and no differentiation was made between IF and RF EMF exposures. This highlights the importance of our results in particular for IF EMF, which although based on a small number of exposed subjects, represent one of the first efforts to study potential risks associated with exposures in this frequency range.

Since radar technologies were developed during World War II, there is a need to balance the benefits and the potential risks associated with the use of these and other technologies that emit RF and/or IF EMF. On one side, RF technologies have had an enormous positive impact on modern society, through multitude of devices for telecommunication and broadcasting, industrial and medical uses, among others. More recently, numerous IF EMF sources, such as those used for identification of items or persons, heating, and other purposes, are becoming progressively common in our environment. However, there is still need to improve the knowledge on the possible negative effects that these technologies may have on health. I hope that the work carried out in this thesis and the results of current and future efforts using the exposure data and the estimates of risks obtained in our studies will help improve this knowledge.

# 6. CONCLUSIONS AND RECOMMENDATIONS

In conclusion, the main assets of this project have been the construction of a database with measurements for the most common sources of EMF exposure in the workplace (OEMD), as well as a source-exposure matrix (SEM) with confidence-weighted mean exposure estimates for all EMF sources identified. Both databases will be publicly available for their use in other epidemiological studies, occupational hygiene programs or the development of new estimates for other purposes. Estimates of the risk of brain tumours due to occupational exposure to RF or IF EMF sources were obtained and will be submitted for publication in a peer-reviewed journal of epidemiology. Although the results found are not sufficiently strong to suggest specific measures or regulatory changes, they add to the current scientific evidence on EMF and health. Nevertheless, in the light of the results and findings described above, I herewith propose the following recommendations:

- The dissemination of exposure measurement data for EMF, as well as for other physical and chemical agents, should be standardized, and efforts should be made to encourage their publication in peer-reviewed journals to improve accessibility. For this purpose, the minimum information required to be included in these publications should be homogenized. This will not only facilitate the work of future exposure data literature reviews, by simplifying the collection and usage of these data in epidemiological and other studies, but will also improve comparability between measurement surveys, allowing a better assessment of their quality and representativeness.
- Efforts should be made in the future to promote the development of more individualized exposure assessment methods for epidemiological studies, either by the collection of personal measurements, if possible, or the development of methodologies such as the source-based approach we

developed for EMF. This will help reduce exposure misclassification by removing or reducing bias, such as that introduced by Berkson-type error.

- The establishment of future occupational and environmental exposure limits for agents such as RF and IF EMF should take into account the potential effects of long-term exposure, by considering the risks estimated in our study and similar previous and future efforts. This will promote the development and implementation of better and more efficient control measures which will help reduce the risks for workers exposed to these fields. In particular, further studies on IF EMF should be encouraged and funding opportunities should be made available in order to improve knowledge on the possible risks from this increasingly present exposure.

# 7. APPENDIX

## Cumulative exposure assessment for sources of high-frequency EMF

### 1. Cumulative exposure metrics for EMF in the literature

Little information exists regarding the development and use of cumulative exposure metrics for electromagnetic fields (EMF). For extremely-low frequency (ELF) exposures, with equal or similar frequencies, μT-year (for magnetic fields) and V/m-year (for electric fields) have been used (IARC, 2002; Turner et al., 2014). For RF, although most recent studies have focused on the development of dose, rather than exposure, metrics such as the specific energy absorption rate (SAR), methods to estimate cumulative exposure to incident fields have been proposed (Baste et al., 2010; Bortkiewicz et al., 1996; Thomas et al., 2008; IARC, 2013) based on the summation of electric fields or ICNIRP ratios, both linearly or squared to consider energy. Because the potential for biological effects is associated with the power deposition and the squares of the electric and magnetic fields are proportional to the power, squared fields have been commonly used in biological sciences (Hitchcock, 2015).

The type and/or magnitude of interaction with biological matter depend on the field frequency (Hitchcock & Paterson, 1995; Röösli, 2014). The International Commission on Non Ionizing Radiation Protection (ICNIRP) proposed the use field ratios as a way to adjust incident electric and magnetic fields to their different frequencies. For this purpose, reference levels (RL) were established for specific fields and frequency ranges for both environmental and occupational exposures, based on well known biological mechanisms (ICNIRP, 1998).

Since the use of frequency-adjusted field ratios might relate better with the interaction with the body, we decided to calculate our estimates of cumulative exposure from different-frequency RF or IF sources using ICNIRP ratios. To do so, mean estimates in the SEM were transformed into ICNIRP ratios using the equation below, based on the RLs in the table below. ICNIRP exposure ratios were obtained by dividing the EMF magnitude G (E-, H- or B-field) over the field reference level (with the same units). Therefore, ratios are unitless. If a source had a frequency range, the field ratio was calculated by obtaining the ratio for the lower and upper bounds and then taking the average. As indicated in the table below, if the RL was a function, *f*, this had to be in the appropriate unit.

$$ICNIRP\_ratio = \left( \frac{G[s,f]}{G_{RL}[s,f]} \right)$$

For the purpose of this study, the sources in the SEM with intermediate frequency (IF) were divided in two groups (IF/ELF, in kHz and IF/RF, in MHz). Only sources in the RF and IF/RF bands were included in this study. For these two bands, squared ratios were used to consider energy (squared fields) rather than incident field.

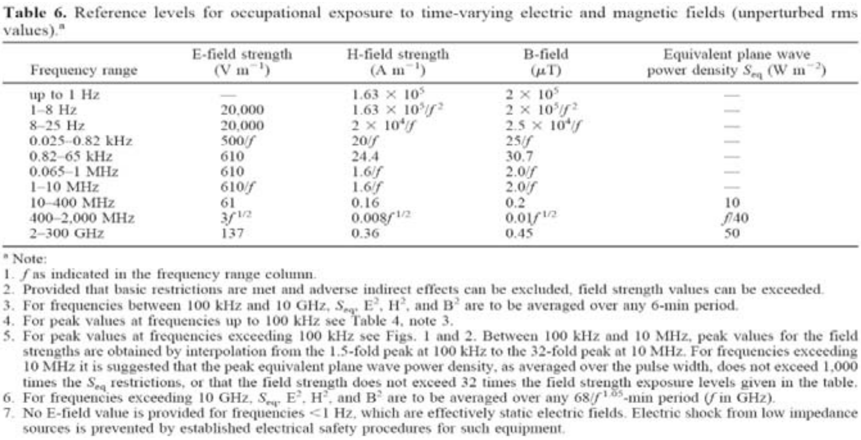


**Table 6.** Reference levels for occupational exposure to time-varying electric and magnetic fields (unperturbed rms values).[a]

| Frequency range | E-field strength (V m$^{-1}$) | H-field strength (A m$^{-1}$) | B-field ($\mu$T) | Equivalent plane wave power density $S_{eq}$ (W m$^{-2}$) |
|---|---|---|---|---|
| up to 1 Hz | — | $1.63 \times 10^5$ | $2 \times 10^5$ | — |
| 1–8 Hz | 20,000 | $1.63 \times 10^5/f^2$ | $2 \times 10^5/f^2$ | — |
| 8–25 Hz | 20,000 | $2 \times 10^4/f$ | $2.5 \times 10^4/f$ | — |
| 0.025–0.82 kHz | $500/f$ | $20/f$ | $25/f$ | — |
| 0.82–65 kHz | 610 | 24.4 | 30.7 | — |
| 0.065–1 MHz | 610 | $1.6/f$ | $2.0/f$ | — |
| 1–10 MHz | $610/f$ | $1.6/f$ | $2.0/f$ | — |
| 10–400 MHz | 61 | 0.16 | 0.2 | 10 |
| 400–2,000 MHz | $3f^{1/2}$ | $0.008f^{1/2}$ | $0.01f^{1/2}$ | $f/40$ |
| 2–300 GHz | 137 | 0.36 | 0.45 | 50 |

[a] Note:

1. $f$ as indicated in the frequency range column.
2. Provided that basic restrictions are met and adverse indirect effects can be excluded, field strength values can be exceeded.
3. For frequencies between 100 kHz and 10 GHz, $S_{eq}$, $E^2$, $H^2$, and $B^2$ are to be averaged over any 6-min period.
4. For peak values at frequencies up to 100 kHz see Table 4, note 3.
5. For peak values at frequencies exceeding 100 kHz see Figs. 1 and 2. Between 100 kHz and 10 MHz, peak values for the field strengths are obtained by interpolation from the 1.5-fold peak at 100 kHz to the 32-fold peak at 10 MHz. For frequencies exceeding 10 MHz it is suggested that the peak equivalent plane wave power density, as averaged over the pulse width, does not exceed 1,000 times the $S_{eq}$ restrictions, or that the field strength does not exceed 32 times the field strength exposure levels given in the table.
6. For frequencies exceeding 10 GHz, $S_{eq}$, $E^2$, $H^2$, and $B^2$ are to be averaged over any $68/f^{1.05}$-min period ($f$ in GHz).
7. No E-field value is provided for frequencies <1 Hz, which are effectively static electric fields. Electric shock from low impedance sources is prevented by established electrical safety procedures for such equipment.

Source: ICNIRP, 1998

## 2. Indices of cumulative RF and IF/RF EMF exposure in INTEROCC

RF or IF/RF EMF exposures with the same intensity may have different effects in the body if they have different frequencies. For instance, both radars and antennas are considered RF sources in INTEROCC. However, a 10 V/m exposure from a 2-MHz antenna may have a different effect than the same exposure level emitted by a 2-GHz radar. To take this potential fact into account, field ratios were calculated for their use in the calculation of indices of cumulative exposure. We assumed that workers are more likely to be exposed to RF or IF/RF EMF sources one by one (sequentially), rather than simultaneously. Therefore, the basic algorithm below was developed to calculate the cumulative exposure index, based on the exposure level accumulated over all the sources reported and the total exposure span (involving duration in years and rate in hours per week/month). Since RF or IF/RF EMF magnetic field (H-field) levels tend to be low and their contribution to internal fields may be small, we decided to use only E-field levels to calculate cumulative exposure indices, as follows:

$$\mathrm{CumE}_{ICNIRP}[\mathrm{i,f}] \approx \sum_{\mathrm{j\,=\,all\ jobs}} \mathrm{Duration[i,j]}\ \frac{\mathrm{Rate}}{S}\mathrm{[i,j]} \sum_{\mathrm{s\,=\,sources\ in\ job\ j}} \overline{\mathrm{E}}^{(2)}_{ICNIRP}[\mathrm{s,f}]\ \mathrm{D[i,j]}\ \mathrm{M[i,j,s]}$$

- where $\overline{\mathrm{E}}^{(2)}_{ICNIRP}[\mathrm{s,f}]$ is an index of the average E-field exposure as the ICNIRP ratio for incident field or associated energy (squared field)*;
- D[i,j] (Distance modifier) and M[i,j,s] (other modifiers) modify the level of exposure. D could only take values (D=1 or D=0) if we considered that exposure to a particular source was feasible within the given distance provided in the questionnaire, where appropriate. Other reported information may modify the exposure intensity differently (e.g. M=1/2);
- Duration[i,j] (in years) and Rate[i,j] (e.g. in hours/day or week) provide the exposure span;
- Because the questionnaire only allowed reporting a value for “rate” once, we couldn´t be sure whether this value referred to the source most frequently used or to an average for all reported sources. Our most conservative choice was to

consider that this Rate referred to the total time worked with all reported sources. Therefore, in order to distribute this rate among all reported sources equally, we considered Rate divided by the total number of sources (S), $\frac{\text{Rate}[i,j]}{S}$.

* $\overline{G}^{(2)}_{ICNIRP}[s,f]$ may, or not, be squared depending on the study hypothesis. Thus, while some authors support that it´s the energy which causes the biological effect, and therefore squares should be used, others maintain that the cause is the actual field, which does not require to be squared.

Because the SEM contains exposure estimates for various dosimetry types, a hierarchy was defined to select the estimates to be used in the algorithm (i.e. personal, operator position, spot, review, expert judgement).

### 3. Simultaneous exposures for RF and IF/ RF EMF

ICNIRP´s guidelines recommends that, when considering simultaneous exposure to different frequency sources, it is important to determine if these exposures are additive in their effects. Moreover, additivity should be considered separately for thermal effects and electrical stimulation. ICNIRP guidelines recommend the following approaches depending on the frequency and biological effect considered:

- ICNIRP, 2010 [1Hz to 100kHz]:
  - linear summation up to 10MHz (nerve stimulation)
- ICNIRP, 1998 [1Hz to 300GHz]:
  - linear summation up to 10MHz (nerve stimulation)
  - sum of squared fields (energy) above 100kHz (thermal effects)

For thermal considerations (>100 kHz), the following method is proposed (ICNIRP, 1998) to estimate multi frequency simultaneous exposures:

$$\sum_{i=100kHz}^{1MHz}\left(\frac{E[s,f]}{c}\right)^2+\sum_{i>1MHz}^{300MHz}\left(\frac{E[s,f]}{E_{RL}[s,f]}\right)^2$$

- where $E[s,f]$ = the electric field from source $s$ with frequency $f$
- $E_{RL}[s,f]$ = the electric field reference level from the table above
- $c = 610/f$ V/m ($f$ in MHz) for occupational exposures
- fields are all squared to consider energy in the summation

In INTEROCC, simultaneous exposure to several different frequency sources at once was only considered feasible for far-field RF-EMF from surrounding antennas and radars. Therefore, the ICNIRP method was used to calculating the integrative exposure from these sources. Thus, the total cumulative-integrative exposure from several RF sources, using the ICNIRP method, was calculated by summing up the ratios from all sources and multiplying this by the exposure span, using the algorithms above.

## 4. Algorithms for specific occupational sections (RF and IF)

The basic model above was used as the basis to assess cumulative exposure for the seven RF and/or IF/RF INTEROCC occupational sections (i.e. radars, transmitters and telecommunication antennas, semiconductors manufacturing, medical diagnosis and treatment, and industrial and food/dental heating). This model was modified to adapt it to the special requirements in some of these seven sections. Details of the specific variables used as modifying factors and/or the modified algorithms for each section, when appropriate, are listed below.

### 4.1 Medical diagnosis and treatment (DxTrt)

In this section, the basic cumulative exposure model was used without modifications or modifying factors.

Simultaneous exposures were not considered in the calculations.

### 4.2 Equipment to cook, dry, sterilise or pasteurise food or to sterilize needles or other medical or dental equipment. (HeatFood)

In this section, the basic model was used without modifications but one modifying factor (i.e. whether the task was automated, done manually or both) was included in the algorithm. When the use of a specific source was automated, we considered that exposure was not likely to happen and the source was not considered in the calculations (M=0). If the source was not automated, exposure was considered possible and it was included in the algorithm (M=1). Finally, if the source was used both automated and manually, the average exposure was considered (M=1/2) for the calculations.

Simultaneous exposures were not considered in the calculations.

### 4.3 Industrial heating equipment to bond, seal or weld materials

In this section, the basic model was used without modifications. Two modifying factors were used:

1. Automated or manually – This factor was treated similarly as above.
2. Hold material in place – Information was collected on whether the material(s) being heated were held or not during the task.

Both modifying factors were used in a decision route to decide whether exposure was likely to happen:

1. Automated = Yes + Hold = No ➔ M=0 (No exposure)
2. Automated = No + Hold =Yes ➔ M=1 (Exposure was plausible)
3. Automated = Yes + Hold = No ➔ *
4. Automated = No + Hold = Yes ➔ *

* For these cases, as well as when not sufficient information was available, decisions were made individually depending on the type of source and other information provided in the questionnaire

Simultaneous exposures were not considered in the calculations.

### 4.4 Manufacturing of semiconductor chips or micro-electronic devices (SCond)

In this section, the basic algorithm was modified to incorporate the effect of using a viewing window during the semiconductors manufacturing process. The modified model takes into account that a portion of the exposed time may include when the subject was looking through a viewing window (assuming an increased exposure during this time). For this ¨viewing¨ portion of time, the assigned exposure is the maximum rather than the mean estimate from the SEM.

$$CumE_{ICNIRP}\ i,f \approx \sum_{j=\text{all}\ jobs} Duration\ i,j \left\{ \delta(view) Rate_{window}\ i,j\ E_{\max}^{ICNIRP}\ s,f + \frac{Rate\ i,j - Rate_{window}\ i,j}{S} \sum_{s=sources\ \text{in}\ job\ j} E_{avg}^{ICNIRP}\ s,f \right\}$$

- where S is the number of sources *without* a viewing window.
- $E_{max}^{ICNIRP}\ s,f$ is the maximum value for the E-field as ICNIRP ratio for the source(s) used with viewing window. $E_{avg}^{ICNIRP}\ s,f$ is the average E-field value (as ICNIRP ratio) for the source(s) used without viewing window.

Two modifying factors were used in this modified algorithm:

1. $M_1 = \delta(view) = 1$ if the source had a viewing window; 0 otherwise
2. $M_3 = Rate_{window} = \dfrac{Viewing\_range\ \ /2\ \frac{1}{60}}{\text{denominator (e.g. 8h, 24h)}}$
3. $M_2$ = Ion current modifier:
    - $M_2 = 0.25$ (Medium current)
    - $M_2 = 4$ (High current)

Simultaneous exposures were not considered in the calculations.

### 4.5 Radar (Radar)

In this section, the basic model was used without modifications. One modifying factor was used to adjust the average E-field exposure level by the distance information provided. Distance from the radar (in m or km) was collected in the questionnaire. This information was used to develop a distance-modifying factor for radars based on the models in Hankin, 1986.

Estimates for radar scenarios in the SEM refer to Near Field (NF) levels (except where indicated). The average distance reported by the subjects was used to assign them on of the boundaries in the table below.

| Boundary | Distance | Unit |
|---|---|---|
| Near field (NF) | $\leq 28$ | m |
| Transition region (IF) | 29-68 | m |
| Far field (FF) | $\geq 69$ | m |

1. If subject is in NF ➔ $D_{NF} = 1$ (direct value from SEM)
2. If subject is in IF ➔ $D_{IF}(R) = (R / R_{NF})^{-1/2}$
3. If subject is in FF ➔ $D_{FF}(R) = 1.57(R / R_{NF})^{-1}$

   - Where R = mean reported distance in m
   - $R_{NF} = 28$ m (Mean distance for NF)

Simultaneous exposures were not considered in the calculations.

### 4.6 Telecommunication antennas (Telcmm Ant)

In this section, the basic model was modified to consider both “worked on” and “surrounding” antennas (simultaneous far-field exposure). Surrounding antennas were considered to lead to simultaneous exposure. Antennas on which the subjects “worked on” were considered to be sequential and were summed up with the resultant of the simultaneous exposure from surrounding antennas.

$$\mathrm{CumE}[i,f] \approx \sum_{j\,=\,\text{all jobs}} \mathrm{Duration}[i,j]\,\frac{\mathrm{Rate}[i,j]}{\mathrm{S}} \sum_{s\,=\,\text{sources in job } j} \left[ (1-\tau)\bar{\mathrm{E}}^{ICNIRP}_{ground}[s,f] + \tau\bar{\mathrm{E}}^{ICNIRP}_{mast}[s,f]_{\;worked-on} + \mathrm{CumE}^{ICNIRP}_{surrounding}[j,f] \right]$$

- where $\tau = ClimbTime$ is the proportion of time reported for climbing antenna masts while broadcasting. $1-\tau$ is the remaining proportion of time working with antennas on the ground.
- $\tau\bar{\mathrm{E}}^{ICNIRP}_{mast}[s,f]_{\;\text{worked-on}}$ is the proportion of exposure from the antenna being climbed, whereas $(1-\tau)\bar{\mathrm{E}}^{ICNIRP}_{\text{ground}}[s,f]_{\;\text{worked-on}}$ is the proportion of exposure from the remaining time not climbing (working with antennas on the ground).
- $\mathrm{CumE}^{ICNIRP}_{surrounding}[j,f]$ is the combined exposure from all surrounding antennas.

For radio broadcasting sources for which there not sufficient information in the interview to determine what type of radio the subject “worked on”, we used the following information (http://www.nationmaster.com/country-info/stats/Media/Radio-broadcast-stations#1998) to assign an antenna scenario from the SEM:

1. UK (1998): AM 219, FM 431, shortwave 3
2. France (1998): AM 41, FM about 3,500 (this figure is an approximation and includes many repeaters), shortwave 2
3. Canada (1998): AM 535, FM 53, shortwave 6

4. Australia (1998): AM 262, FM 345, shortwave 1
5. Germany (1998): AM 51, FM 787, shortwave 4
6. Israel (1998): AM 23, FM 15, shortwave 2
7. New Zealand (1998): AM 124, FM 290, shortwave 4

When the radio frequency band could not be determined, we used a weighted average of the AM and FM SEM entries, using:

$$E_{\text{radio broadcasting}} = n_{AM}E_{AM} + n_{FM}E_{FM} \Big/ n_{AM} + n_{FM}$$

- where the weights $n_{AM}$ and $n_{FM}$ are the number of licenses in the subject's country, as below:
- AM = 526.5 kHz–1.6065 MHz (IF-RF)
- Shortwave = 2.3–26.1 MHz (RF, HF)
- FM = 87.5 to 108.0 MHz (RF, VHF)

The only modifying factor was $\tau = ClimbTime$ (Proportion of time climbing energized antennas). Exposure level is obtained through scenarios so no other modifying factors are required. If the question on Climb=Yes, we assumed that antennas were broadcasting/energized.

For simultaneous antennas, we used the ICNIRP method for different frequency sources as described above.

### 4.7 Transmitters

In this section, the basic model was used with no modifications. Three modifying factors were considered:

1. Transmitter use:
    - At work ➔ $M_1$=1 (exposure was considered plausible)
    - Outside work ➔ $M_1$=0 (source was considered non-occupational)
    - Both ➔ $M_1$=1/2 (half the exposure rate was assigned)

2. Transmitter location
    - On the handset into which you speak ➔ $M_2$=1 (full exposure)
    - On a device carried on your body ➔ $M_2$=0 (We assumed that this was a personal device with a not very powerful antenna, and little or no exposure to the brain)
    - Mounted on a vehicle (such as a car or truck) ➔ Exposure depends on the location of the antenna on the vehicle. See below.

3. Antenna location
    - Outside the vehicle ➔ $M_3$=0
    - Inside the vehicle, within 10 cm from your head or body ➔ $M_3$=1

- Inside the vehicle, further than10 cm from your head or body ➔ $M_3$=0 (We assume that this is a personal device with not a very powerful antenna).
    - Exception: For CBs ➔ $M_3$=1/2 (We assumed that CBs have more powerful antennas).
- Elsewhere:
    - 10-15cm from head or body ➔ M3=1
    - >10-15cm from head or body ➔ M3=0
        - Exception: For CBs (TrsmtType=1) ➔ M3=1/2 (The same as above).

Simultaneous exposures were not considered in the calculations.

## 5. Results

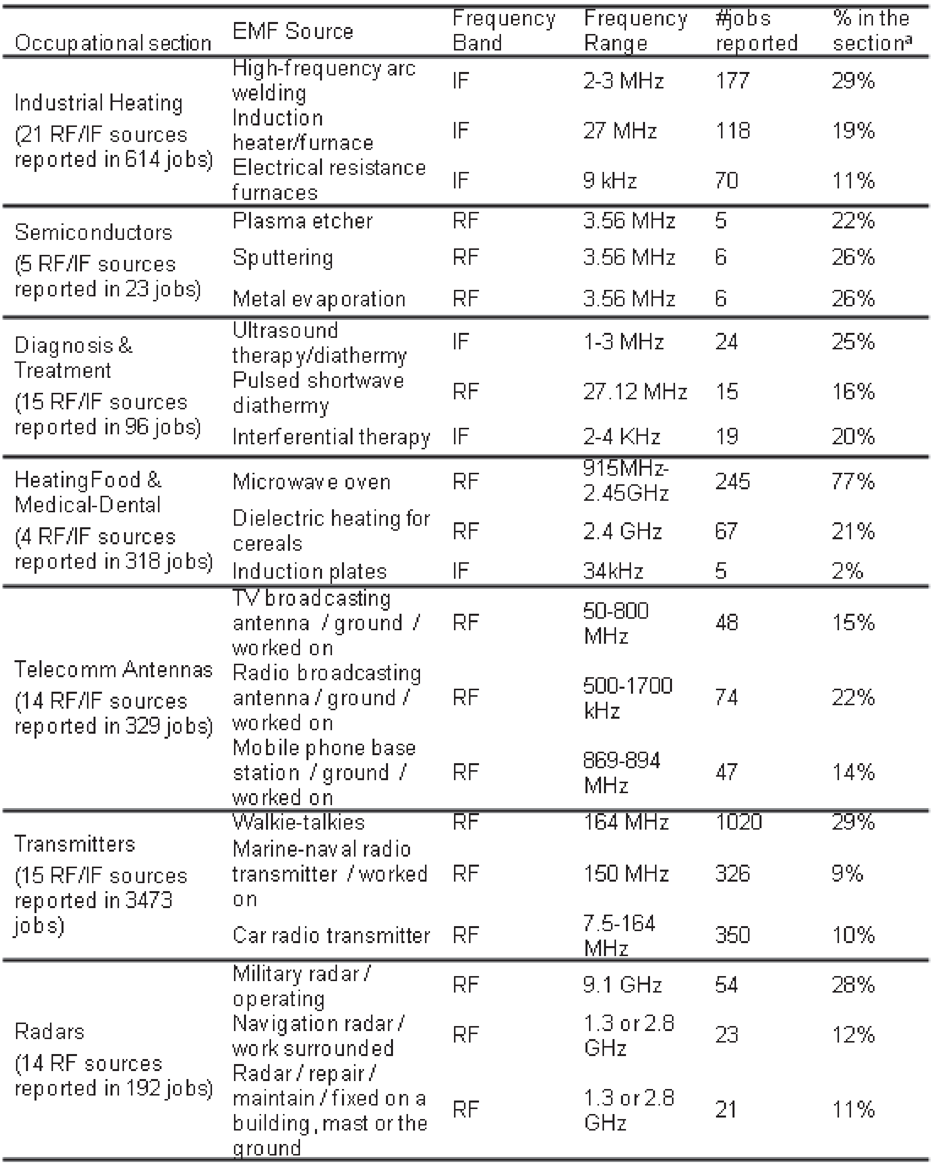
The ratio of the mean electric field to the ICNIRP guidelines for both RF and IF EMF sources measured at the operator position ranged from $2.79\times10^{-4}$ (semiconductor etchers) to 6.02 (RF plastic heat sealer), while the maximum spot measurement was 82.0 times ICNIRP's electric field guidelines near continuous short-wave diathermy equipment. The sources most frequently reported (Table 1) were microwave oven (77% of food heating equipment) walkie talkies (29% of transmitters), and high-frequency arc welding (29% of industrial heating equipment).

A total of 9.1% of the 9,579. INTEROCC subjects reported working with RF sources such as radar, broadcasting, telecommunications, semiconductor manufacturing, medical diagnosis and treatment, the heating and bonding of industrial materials, and food preparation. Their cumulative exposures to RF electric fields had a third quartile 89.7 times above the first quartile (interquartile ratio).

## 6. Incident field exposure metrics versus dosimetric modeling

The use of ICNIRP ratios as an "exposure metric" has advantages and disadvantages as a method of pooling exposures over multiple frequencies and across the RF and IF/RF frequency bands. ICNIRP reference levels account for the frequency dependency of the coupling of electric and magnetic fields with the body to produce internal electric fields. However, ICNIRP ratios have been developed as a metric for compliance with a regulatory limit, rather than an exposure metric, and there is no evidence that their use may have biophysical meaning. Therefore, future exposure/dose modeling efforts will include the development of metrics based on Basic Restrictions for internal electric fields and SAR for RF and IF/RF EMF (>100kHz) [ICNIRP, 1998].

Table 1 – Distribution of RF/IF sources most frequently reported by study subjects



| Occupational section | EMF Source | Frequency Band | Frequency Range | #jobs reported | % in the section$^a$ |
|---|---|---|---|---|---|
| Industrial Heating<br>(21 RF/IF sources reported in 614 jobs) | High-frequency arc welding | IF | 2-3 MHz | 177 | 29% |
| | Induction heater/furnace | IF | 27 MHz | 118 | 19% |
| | Electrical resistance furnaces | IF | 9 kHz | 70 | 11% |
| Semiconductors<br>(5 RF/IF sources reported in 23 jobs) | Plasma etcher | RF | 3.56 MHz | 5 | 22% |
| | Sputtering | RF | 3.56 MHz | 6 | 26% |
| | Metal evaporation | RF | 3.56 MHz | 6 | 26% |
| Diagnosis & Treatment<br>(15 RF/IF sources reported in 96 jobs) | Ultrasound therapy/diathermy | IF | 1-3 MHz | 24 | 25% |
| | Pulsed shortwave diathermy | RF | 27.12 MHz | 15 | 16% |
| | Interferential therapy | IF | 2-4 KHz | 19 | 20% |
| HeatingFood & Medical-Dental<br>(4 RF/IF sources reported in 318 jobs) | Microwave oven | RF | 915MHz-2.45GHz | 245 | 77% |
| | Dielectric heating for cereals | RF | 2.4 GHz | 67 | 21% |
| | Induction plates | IF | 34kHz | 5 | 2% |
| Telecomm Antennas<br>(14 RF/IF sources reported in 329 jobs) | TV broadcasting antenna / ground / worked on | RF | 50-800 MHz | 48 | 15% |
| | Radio broadcasting antenna / ground / worked on | RF | 500-1700 kHz | 74 | 22% |
| | Mobile phone base station / ground / worked on | RF | 869-894 MHz | 47 | 14% |
| Transmitters<br>(15 RF/IF sources reported in 3473 jobs) | Walkie-talkies | RF | 164 MHz | 1020 | 29% |
| | Marine-naval radio transmitter / worked on | RF | 150 MHz | 326 | 9% |
| | Car radio transmitter | RF | 7.5-164 MHz | 350 | 10% |
| Radars<br>(14 RF sources reported in 192 jobs) | Military radar / operating | RF | 9.1 GHz | 54 | 28% |
| | Navigation radar / work surrounded | RF | 1.3 or 2.8 GHz | 23 | 12% |
| | Radar / repair / maintain / fixed on a building, mast or the ground | RF | 1.3 or 2.8 GHz | 21 | 11% |

[a] This percentage refers to the jobs in which work with or surrounded by RF/IF sources were reported.

## 7. References

- Baste V, Mild KH, Moen BE. Radiofrequency exposure on fast patrol boats in the Royal Norwegian Navy--an approach to a dose assessment. Bioelectromagnetics. 2010;31(5):350-60.

- Bortkiewicz A, Gadzicka E, Zmyślony M. Heart rate variability in workers exposed to medium-frequency electromagnetic fields. J Auton Nerv Syst. 1996;59(3):91-7.

- Hankin NN. (1986) The radiofrequency radiation environment: environmental exposure levels and RF radiation emitting sources. Washington, DC: Environmental Protection Agency (EPA). Available at http://nepis.epa.gov/EPA/html/DLwait.htm?url=/Exe/ZyPDF.cgi/2000ECTQ.PDF?Dockey=2000ECTQ.PDF. Accessed 22 June 2016.

- Hitchcock RT, Patterson RM. (1995) Radio-frequency andELF electromagnetic energies: a handbook for health professionals. New York, NY: Van Nostrand Reinhold. ISBN: 9780471284543.

- Hitchcock RT. Radio-Frequency Radiation. In: Hamilton and Hardy's Industrial Toxicology, Sixth Edition. Edited by Raymond D. Harbison, Marie M. Bourgeois, and Giffe T. Johnson. 2015 John Wiley & Sons, Inc.

- IARC. Non-ionizing radiation, Part 1: Static and extremely low-frequency (ELF) electric and magnetic fields. IARC Monogr Eval Carcinog Risks Hum. 2002;80: 1–395.

- IARC. Non-ionizing radiation, Part 2: Radiofrequency electromagnetic fields. IARC Monogr Eval Carcinog Risks Hum. 2013;102: 1–460.

- ICNIRP. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). International Commission on Non-Ionizing Radiation Protection. Health Phys. 1998;74(4):494-522.

- ICNIRP. Guidelines for limiting exposure to time-varying electric and magnetic fields (1 Hz to 100 kHz). International Commission on Non-Ionizing Radiation Protection. Health Phys. 2010;99(6):818-36.

- Kaune, WT (2002). Estimating the magnitude of the sum of two magnetic fields with uncertain spatial orientations, polarizations, and/or relative phase. Bioelectromagnetics, 23, 59-67.

- Röösli M. (2014) Epidemiology of electromagnetic fields. Boca Raton; London; New York: CRC Press. ISBN: 9781466568167.

- Thomas S, Kühnlein A, Heinrich S, Praml G, Nowak D, von Kries R, Radon K. Personal exposure to mobile phone frequencies and well-being in adults: a cross-sectional study based on dosimetry. Bioelectromagnetics. 2008;29(6):463-70.

- Turner MC, Benke G, Bowman JD et al. Occupational exposure to extremely low-frequency magnetic fields and brain tumor risks in the INTEROCC study. Cancer Epidemiol Biomarkers Prev. 2014;23:1863–72.

## 8. SUPPLEMENTAL MATERIAL FOR PAPER II

### Statistical Methods Developed for the INTEROCC Study's Assessment of EMF Exposures

by J.D. Bowman and J. Vila

***for the manuscript***

"Development of a source-exposure matrix for occupational exposure assessment of electromagnetic fields in the INTEROCC Study" by Vila, Bowman et al.

**Published in the *J Expo Sci Environ Epidemiol.***

### *Summary*

We here derive the formulas for calculating the confidence-weighted arithmetic means (*AM*), geometric means (*GM*) and their corresponding standard deviations (*SD* and *GSD*) from EMF data obtained from the Occupational Exposure Measurement Database (OEMD). In part A of this appendix, we derive the formulas in Tables 1 and 2 for estimating summary statistics which are not in OEMD. Part B contains derivations for the confidence weighted means and standard deviations from OEMD's summary statistics

### A. *Semi-empirical methods for estimating summary statistics for the SEM*

The problem is to estimate these statistics from sparse information, typically the minimum (*Min*) and maximum (*Max*) but also the number of measurements (*N*), arithmetic or geometric mean, and outside-dynamic-range values (*ODRMin* or *ODRMax*). Our solution is to derive the summary statistics from the assumption that the exposure data are distributed log-normally, and any unknown variable (such as the *GSD*) needed to complete the derivation is replaced with its central tendency calculated from an appropriate data set – a semi-empirical approach.

This approach is an extension of the expert judgment method developed by Bowman, Sivaganesan, Shulman and Cardis [2013], which starts with the log-normal relationships for the standard normal quantiles, *z,* corresponding to *Min* and *Max*:

$$\ln Min = \ln GM + z_{\mathrm{Min}} \ln GSD \qquad \text{(A1a)}$$

$$\ln Max = \ln GM + z_{Max} \ln GSD \qquad \text{(A1b)}$$

By adding and subtracting these two equations, Bowman et al. [2013] derived formulas for estimating *GM* and *GSD* as functions of *Min* and *Max*:

$$\widehat{lnGM} = \ln GME - \frac{\alpha}{2}\left(\ln Max - \ln Min\right) \qquad \text{(A2a)}$$

$$\widehat{lnGSD} = \frac{1}{2\zeta}\left(\ln Max - \ln Min\right) \tag{A2b}$$

where the hat designates estimates and the symbols α, ζ, and *GME* are defined as:

$$\begin{aligned} \alpha &\equiv \frac{z_{\text{Max}} + z_{\text{Min}}}{z_{\text{Max}} - z_{\text{Min}}} \\ \zeta &\equiv \tfrac{1}{2}\left(z_{\text{Max}} - z_{\text{Min}}\right) \end{aligned} \tag{A3}$$

$$\begin{aligned} GME &= \text{ geometric mean of the extremes} \\ &\equiv \sqrt{Max * Min} \end{aligned} \tag{A4}$$

The parameter α is an asymmetry parameter that measures how far $z_{\text{Min}}$ and $z_{\text{Max}}$ deviate from being symmetric about zero (*i.e.* $z_{Min} = - z_{Max}$). ζ is the average distance of $z_{\text{Min}}$ and $z_{\text{Max}}$ from the mean of the log-transformed data, and therefore serves as the "effective quantile" in the estimation formula for the *GSD* (eq. A2b). *GME*, the geometric mean of the extreme values (*Min* and *Max*), has a long history, which we traced back from Enrico Fermi through Voltaire, Sir Isaac Newton and Euclid to the Pythagorean mathematician Archytas in the fifth century BCE [Bowman and Vila, unpublished].

In expert judgment studies, values for *Min* and *Max* are elicited from an expert panel, which provides values for two of the four variables on the right hand side of the two equations for *GM* and *GSD* (eqs. A2). The two remaining unknown variables, α and ζ, are the semi-empirical parameters, whose central tendencies $\bar{\alpha}$ and $\bar{\zeta}$ (means or medians as best fits the calibration data) are calculated from the expert judgment results with a calibration data set whose *GM* and *GSD* are known. After determining $\bar{\alpha}$ and $\bar{\zeta}$, estimated summary statistics, $\widehat{GM}$ and $\widehat{GSD}$, can then be calculated for exposures beyond the calibration set with eqs. A1, using only their *Min* and *Max*. Next, the *AM* and *SD* are derived from the exact relationships between the statistics of a log-normal distribution [Aitchison and Brown, 1957]:

$$\ln AM = \ln GM + \tfrac{1}{2}\ln^2 GSD \tag{A5}$$

$$SD = \frac{AM}{GM}\sqrt{AM^2 - GM^2} \tag{A6}$$

Formulas for all the statistics in the expert judgment method are in the first row of Table A-I. Note that the formulas in Table A-I are the anti-logs of eqs. A2 and A6, which results in more compact equations with greater computational efficiency.

*Summary statistics from OEMD data*

A similar approach is used to estimate summary statistics with data from OEMD, although the formalism is made more complicated by the many combinations of *Min*, *Max, AM, GM, N, ODRMin,* and/or *ODRMax* whose values were extracted into OEMD from different publications. In order to structure a semi-empirical derivation of formulas for all the summary statistics, we start with a theorem from algebra that a system of simultaneous polynomial equations has solutions if the number of equations equals the number of unknown variables.

With the formalism outlined above, there are 2 linear equations (eqs. A2a and A2b). (Note that the log-transformed statistics like ln *GM* and ln *Min* are treated as the variables in order to make these equations linear). If eq. A4 is substituted into eq. A2a, these two have a total of 6 linear variables (ln *GM,* ln *GSD,* ln *Max,* ln *Min,* $\alpha$ and $\zeta$). Since values for *Max* and *Min* are provided by the expert panel, only four of the variables are unknown, but this is greater than the number of equations, leaving their solution underdetermined. In order to evaluate the formal solutions for the unknowns, $\widehat{lnGM}$ and $\widehat{lnGSD}$ in eqs. A2, the expert judgment method therefore provided values for the 2 semi-empiric variables $\alpha$ and $\zeta$. This reasoning can be expressed numerically as:

2 equations = 2 unknowns = 6 total variables – 2 variables with values – 2 semi-empiric variables (A7)

An algebraic form of eq. A7 can be re-arranged into a general expression for the number of semi-empiric variables needed to solve a system of simultaneous equations:

$$s = t - m - v \tag{A8}$$

where $s$ = number of semi-empiric variables, $t$ = total number of variables, $m$ = number of equations, and $v$ = number of variables with values.

To illustrate the application of this semi-empirical method to OEMD data, consider a record with values for *Min* and *Max*, so there are $v$=2 variables with values (method #2 in Table A-I). To obtain estimates for *GM* and *GSD*, we use eqs. A2a and A2b, creating a system of $m$=2 simultaneous equations with $t$ = 6 variables. According to eq. A8, values are needed for $s$ = 2 semi-empiric variables in order to solve these two equations for the unknown summary statistics.

The first semi-empiric variable is provided by assuming $z_{Min} = -z_{Max}$, so that $\alpha$= 0 (eq. A-3). We call this "the symmetric quantile" assumption because the minimum and maximum quantiles are symmetric about zero (the mean quantile), and the corresponding percentiles also have the symmetry $P_{Min} = 1 - P_{Max}$, (e.g. the 5th and 95th percentiles). The symmetric quantile assumption makes eq. A2a into $\widehat{lnGM} = \ln GME$, whose anti-log is the estimation formula in Table A-I.

From the definitions of $\alpha$ and $\zeta$ (eqs. A3), this assumption also implies that $z_{Max} = -z_{Min} = \zeta$, so eq. A2b becomes ln $\widehat{GSD}$ = (ln *Max* – ln *Min*)/2$z_{Max}$. A solution for $\widehat{GSD}$ therefore requires the second semi-empiric parameter $\overline{z_{Max}}$ , where the bar represents the central tendency of $z_{Max}$ calculated exactly from the formula in Table A-I from OEMD records with $v$=3. With semi-empiric estimates for $\widehat{GM}$ and $\widehat{GSD}$, *AM* and *SD* can now be estimated with the relationships A5 and A6 between exact values for the summary statistics of a log-normal distribution, as shown for method #2 in Table A-I.

Note that the formulas for *SD* in Table A-I only require values for *AM* and *GM,* which are either input values or have already been estimated by the other formulas in Table A-I. Since the same situation applies to all other combinations of input data in Tables A-I and A-II, slight variations of eq. A6 are used to estimate *SD* throughout the SEM calculations.

With 2 or less variables with values in an OEMD record, semi-empiric values are needed in addition to the $\alpha = 0$ assumption to obtain solutions for the missing summary statistics. As shown in Table A-I, $v$ = 2 values for *Max* and *Min* requires a central tendency for $\overline{z_{\text{Max}}}$ in order to estimate the summary statistics, while a record with a value for only *Max* ($v = 1$) requires an additional central tendency for $\overline{GSD}$. These central tendencies are calculated from a sub-set of OEMD records with values for enough variables for the simultaneous equations to have exact solutions (i.e. $s \leq 0$). Whether the median, AM or GM is the best central tendency for these semi-empiric parameters is addressed in the main paper.

*Summary statistics from OEMD data that include N*

In addition to the summary statistics examined above, some OEMD records also contained the number of measurements *N* used to calculate the statistics. To employ the reported *N* values in our summary statistic estimates, $z_{\text{Max}}$ and $z_{\text{Min}}$ are equated to their expected values for a sample of *N* quantiles *z* from the standard normal distribution (Zwillinger and Kokoska 2000). When the *N* expected values $E_N[z]$ are ranked according to their values, these “expected normal order statistics” [also called “rankits” by Ipsen and Jerne (1944)] are widely used in normal probability plots (Snedecor and Cochran, 1989).

In the SEM calculations, the expected normal order statistics for the extreme quantiles, $E_N[z_{\text{Max}}]$ and $E_N[z_{\text{Min}}]$, are calculated by a numeric algorithm (Royston, 1982) and assumed to equal the actual minimum and maximum quantiles for OEMD records that have values for the sample size *N*:

$$z_{\text{Min}} = E_N[z_{\text{Min}}] \tag{A9a}$$

$$z_{\text{Max}} = E_N[z_{\text{Max}}] \tag{A9b}$$

In addition, the extremes of the expected normal order statistics for a given *N* are symmetric (Zwillinger and Kokoska 2000):

$$E_N[z_{\text{Min}}] = - E_N[z_{\text{Max}}] \tag{A10}$$

In other words, they fulfil the symmetric quantile ($\alpha = 0$) assumption.

Using these results in the summary statistics calculations, there are now $n = 6$ simultaneous equations (eqs. A1a, A1b, A5, A9a, A9b and A10) with 2 additional variables with values ($E_N[z_{\text{Min}}]$ and $E_N[z_{\text{Max}}]$ ), giving a total of $t = 9$ variables. When OEMD has *Min, Max* and *AM* in addition to *N,* the number of variables with values is now $v = 5$, so eq. A8 now gives $s = -1$. This negative result means there are more simultaneous equations than unknown variables, so this over-determined system of equations has more than one solution for both *AM* and *GM* in Table A-II. The common-sense resolution to this “embarrassment of riches” is to set *AM* equal to the reported *AM*, rather than use the solution: $AM = GME\sqrt{GSD^{\ln GSD}}$ derived from the 6 simultaneous equations.

Estimation formulas for other data combinations in OEMD that include *N* are given in Table A-II.

**Table A-I.** Formulas for estimating summary statistics from expert judgments for *Min* and *Max* and from OEMD data for *Min, Max, AM* and *GM*.

| Input values | Estimate | Formula |
|---|---|---|
| Method #0: $v = 2$ values, $m = 2$ equations (eqs. A2a & A2b), $s = 2$ semi-empiric parameters ($\alpha$ and $\zeta$) | | |
| *Min & Max* | $\widehat{GM} =$ | $GME \Big/ \left(\sqrt{Max/Min}\right)^{\overline{\alpha}}$ where $GME \equiv \sqrt{Max * Min}$ |
| | $\widehat{GSD} =$ | $\left(\sqrt{Max/Min}\right)^{1/\overline{\zeta}}$ |
| | $\widehat{AM} =$ | $\widehat{GM}\sqrt{\widehat{GSD}^{\widehat{GSD}}}$ |
| | $\widehat{SD} =$ | $\frac{\widehat{AM}}{\widehat{GM}}\sqrt{\widehat{AM}^2 - \widehat{GM}^2}$ |
| Method #1: $v = 3$ values, $m = 3$ equations (eqs. A2a, A2b & A5), $s = 1$ assumption ($\alpha = 0$) | | |
| *Min, Max & AM* | $\widehat{AM} =$ | $AM$ |
| | $\widehat{z_{Max}} =$ | $\ln\left(Max/Min\right) \Big/ 2\sqrt{\ln\left[AM^2/\left(Min * Max\right)\right]}$ |
| | $\widehat{GSD} =$ | $\left(\sqrt{Max/Min}\right)^{1/\widehat{z_{Max}}}$ |
| | $\widehat{GM} =$ | $\mathrm{AM} \Big/ \sqrt{\widehat{GSD}^{\ln \widehat{GSD}}}$ |
| | $\widehat{SD} =$ | $\frac{AM}{\widehat{GM}}\sqrt{AM^2 - \widehat{GM}^2}$ |
| Method #2: $v = 2$ values, $m = 3$ equations, $s = 2 = 1$ assumption ($\alpha = 0$) + 1 semi-empiric parameter ($z_{\mathrm{Max}}$) | | |
| *Min & Max* | $\widehat{GM} =$ | $GME$ |
| | $\widehat{GSD} =$ | $\left(\sqrt{Max/Min}\right)^{1/\overline{z_{\mathrm{Max}}}}$ |
| | $\widehat{AM} =$ | $\widehat{GM}\sqrt{\widehat{GSD}^{\widehat{GSD}}}$ |
| | $\widehat{SD} =$ | $\frac{\widehat{AM}}{\widehat{GM}}\sqrt{\widehat{AM}^2 - \widehat{GM}^2}$ |
| Method #3: $v = 1$ value, $m = 3$ equations, $s = 3 = 1$ assumption ($\alpha = 0$) + 2 semi-empiric parameters ($z_{\mathrm{Max}}$ & $GSD$) | | |
| *Max** | $\widehat{GM} =$ | $Max \Big/ \overline{GSD}^{\overline{z_{\mathrm{Max}}}}$ |
| | $\widehat{AM} =$ | $Max\sqrt{Q^{-2\overline{z_{\mathrm{Max}}}}}$, where $Q = \overline{GSD}^{\ln \overline{GSD}}$ |
| | $\widehat{GSD} =$ | $\overline{GSD}$ |
| | $\widehat{SD} =$ | $\frac{\widehat{AM}}{\widehat{GM}}\sqrt{\widehat{AM}^2 - \widehat{GM}^2}$ |

Note: The formulas for the estimated statistics, designated by hats, are re-defined for each method. Therefore, applications of estimated statistics in subsequent formulas have values defined for the same method with the given set of input data. The only statistics whose values are the same in multiple methods are the central tendencies for $z_{Max}$ and *GSD*, designated by bars.

*Formulas when *Min* is the only input are not given because this case does not occur in OEMD.

**Table A-I.** Concluded.

| Input values | Estimate | Formula |
|---|---|---|
| Methods #4 and 5: $v$ = 1 value (*AM* or *GM*), $m$ = 1 equation (eq. A5), $s$ = 1 semi-empiric parameter (*GSD* or Q) | | |
| *AM* | $\widehat{AM}$ = | $AM$ |
| | $\widehat{GM}$ = | $AM \big/ \sqrt{Q}$ |
| | $\widehat{GSD}$ = | $\overline{GSD}$ |
| | $\widehat{SD}$ = | $\frac{AM}{\widehat{GM}}\sqrt{AM^2 - \widehat{GM}^2}$ |
| *GM* | $\widehat{GM}$ = | $GM$ |
| | $\widehat{AM}$ = | $GM\sqrt{Q}$ |
| | $\widehat{GSD}$ = | $\overline{GSD}$ |
| | $\widehat{SD}$ = | $\frac{\widehat{AM}}{GM}\sqrt{\widehat{AM}^2 - GM^2}$ |

**Table A-II.** Formulas for estimating summary statistics from OEMD data that include *N*.

| Input values | Estimate | Formula |
|---|---|---|
| Method #1′: *v* = 5 values, *m* = 6 equations (eqs. A1a, A1b, A5, A8a, A8b & A9), *s* = -1 (over-determined solutions) | | |
| *N, Min, Max & AM* | $\widehat{AM}$ = | $AM$ or $GME\sqrt{\widehat{GSD}^{\widehat{GSD}}}$ |
| | $\widehat{GSD}$ = | $\left(\sqrt{Max/Min}\right)^{1/E_N[z_{Max}]}$ |
| | $\widehat{GM}$ = | $GME$ or $\mathrm{AM}\Big/\sqrt{\widehat{GSD}^{\ln\widehat{GSD}}}$ |
| Method #2′: *v* = 4 values, *m* = 6 equations, *s* = 0 (exact solution) | | |
| *N, Min & Max* | $\widehat{GM}$ = | $GME$ |
| | $\widehat{GSD}$ = | $\left(\sqrt{Max/Min}\right)^{1/E_N[z_{Max}]}$ |
| | $\widehat{AM}$ = | $\widehat{GM}\sqrt{\widehat{GSD}^{\widehat{GSD}}}$ |
| Method #3′: *v* = 3 values, *m* = 6 equations, *s* = 1 semi-empiric parameters (*GSD*) | | |
| *N & Max* | $\widehat{GM}$ = | $Max\Big/\overline{GSD}^{E_N[z_{Max}]}$ |
| | $\widehat{AM}$ = | $Max\sqrt{Q^{-2E_N[z_{Max}]}}$, where $Q=\overline{GSD}^{\ln\overline{GSD}}$ |
| | $\widehat{GSD}$ = | $\overline{GSD}$ |

Thus, for OEMD records with $N$, two alternative methods in Tables A-I and II provide estimates for the unknown summary statistics for OEMD data combinations #1, 2 and 3. Comparing methods in these two tables, their formulas are identical, except for the exponents of $\widehat{GSD}$ in methods 1 and 2 and the exponents of $\widehat{AM}$ and $\widehat{GM}$ in method 3. Those exponents contain $\widehat{z_{Max}}$ or $\overline{z_{Max}}$ in Table A-I, but are replaced with $E_N[z_{Max}]$ in Table A-II. Those exponents do not appear explicitly in methods 4 and 5.

In deciding which methods to use for the SEM calculations, we first note that methods in Table A-II have the additional assumption that the extreme quantiles for an OEMD record equal their expected values for the reported sample size $N$ (eqs. A9). In order to evaluate the effects of this "expected quantile assumption," we used the Monte Carlo simulations described in the main paper. Those simulations take 10,000 samples of $N$ measurements from a log-normal distribution with $GM = 20$ and $GSD = 2.5$, where $N$ for each simulation is a random selection from all values in OEMD. From these simulated data, we calculated the overall uncertainty in the estimated summary statistics (as described in the Methods of the main paper) with the methods in Tables A-I and A-II. From the simulation results, we chose the methods with the lower overall uncertainty for the arithmetic and geometric means to use in the SEM calculations.

The resulting overall uncertainties for the two alternative exponents are given in Table A-III. The minimum uncertainty for the means are achieved with the exponent $E_N\,[z_{Max}]$ for methods #1 and 3, but with $\overline{z_{Max}}$ for method #2. These optimal exponents are used in the estimation formulas for both the SEM calculations (Table 1) and the validation calculations (Table 5).

Note that the uncertainty pattern for the standard deviations in Table A-III are somewhat different than for the means. In selecting the optimal methods, we focused on the mean estimates since only the SEM means are needed for obtaining risk estimates, which are INTEROCC's primary objectives. We included the uncertainties in the standard deviations in Table A-III and Table 5, so that they can be taken into account by any future studies of the variabilities and uncertainties in the risk estimates by simulations with the SEM.

### *Statistics for measurements outside the meter's dynamic range*

The last type of record in OEMD are from studies which report measurements outside the meter's dynamic range. In these cases, *Min* or *Max* are replaced with the dynamic range's lower limit (ODR*Min*) or upper limit (ODR*Max*). In those cases, we model the actual *Min* or *Max* with the reported ODR values times empirical parameters $k_{under} < 1$ and $k_{over} > 1$:

$$\widehat{Min} = ODRMin * \widehat{k_{under}} \tag{A11a}$$

$$\widehat{Max} = ODRMax * \widehat{k_{over}} \tag{A11b}$$

Initially, we were able to calculate an average $k_{over}$ empirically based on data from two sets of measurements of personal exposures to a magnetic field source using two different ENERTECH EMF

**Table A-III.** Simulated uncertainties of the alternative estimation formulas in Tables A-I and A-II with the lower uncertainty for each combination of the estimated statistic and method in **bold**.

| **Estimated statistic** | **Exponent alternatives*** | **Overall uncertainty of the estimated statistics by method # (with the OEMD statistics used)** | | |
|---|---|---|---|---|
| | | **1(AM, *Min & Max*)** | **2(*Min & Max*)** | **3(*Max*)** |
| $\widehat{GM}$ | $z_{Max}$ | 51% | **53%** | 212% |
| | $E_N[z_{Max}]$ | **47%** | **53%** | **143%** |
| $\widehat{AM}$ | $z_{Max}$ | | **125%** | 166% |
| | $E_N[z_{Max}]$ | | 682% | **88%** |
| $\widehat{GSD}$ | $z_{Max}$ | 75% | 75% | **78%** |
| | $E_N[z_{Max}]$ | **33%** | **33%** | **78%** |
| $\widehat{SD}$ | $z_{Max}$ | **185%** | **593%** | **894%** |
| | $E_N[z_{Max}]$ | 1793% | 262,450% | 2098% |

*In the simulations, these alternatives were used as $\widehat{z_{Max}}$ for estimation method #1, and as $\overline{z_{Max}}$ in methods #2 and 3.

meters (http://www.enertech.net), a Standard EMDEX II (*ODRMax*=300 µT) and a Hi-Field EMDEX II (*ODRMax* = 12,000 µT). However, no such data were available for EMF measurements below a meter's limit of detection, so we needed a semi-empirical approach to obtain $k_{under}$. We identified two suitable methods by using the same assumptions (a log-normal distribution and $\alpha = 0$) and similar algebra to the derivations above.

In the first approach, the input data are ODR*Min* and *Max*, so eqs. A1 and A11a are adequate to derive $k_{under}$ with the semi-empirical methods described above. The $m$=2 simultaneous equations are:

$$lnODRMin + ln\widehat{k_{under}} = ln\widehat{GM} - \widehat{z_{Max}}ln\widehat{GSD} \tag{A12a}$$

$$lnMax = ln\widehat{GM} + \widehat{z_{Max}}ln\widehat{GSD} \tag{A12b}$$

These equations have a total of $t$ = 6 variables of which $v$ = 2 have values, so they can be solved for the summary statistics with $s$ = 2 semi-empiric values for $z_{Max}$ and *GSD*.

$$\widehat{k_{over}} = \frac{Max}{ODRMin * \overline{GSD}^{\overline{z_{Max}}}} \tag{A13a}$$

$$\widehat{GM} = \sqrt{\widehat{k_{under}} * ODRMin * Max} \tag{A13b}$$

This approach gives specific values for $k_{under}$ with each OEMD record reporting ODR*Min*, but the results for $k_{under}$ were often greater than 1, a violation of the model's assumptions and therefore implausible.

In the second approach, a sub-set of the ODRMin records were used that also have a value for *AM*. By adding eq. A5 to the set of simultaneous equations (eq. A12), we derive a different formula for $k_{under}$ with only one semi-empirical parameter as follows:

Add eqs. A12a and A12b, and re-arrange to give:

$$ln\widehat{GM} = \frac{1}{2}\left(lnMax + ln\widehat{k_{under}} + lnODRMin\right) \tag{A14}$$

Now, substitute eq. A14 for ln *GM* in eq. A5, use the semi-empirical parameter $\overline{GSD}$, solve for ln $k_{under}$, and take the anti-log to obtain the desired result:

$$\widehat{k_{under}} = \frac{AM^2}{Max * ODRMin * \sqrt{Q}} \tag{A15}$$

With this approach, the mean of $k_{under}$ over the sub-set is less than one, which allows for realistic estimates of the GM for each ODR*Min* record from the ODR equivalent of the *GME* (eq. A4):

$$\widehat{GM} = \sqrt{k_{under} * ODRMin * Max} \tag{A16}$$

The other statistics for these ODR*Min* records are then calculated with analogs of the $m = 2$ formulas in Table A-I. The resulting formulas are reported in Table 2 in the main paper.

### B. *Confidence-Weighted Means and Standard Deviations for the SEM*

For each source in OEMD, the exposure statistics $AM_i$, $SD_i$, $GM_i$ and $GSD_i$ for all applicable records $i$ are pooled with confidence weights $C_i$. To derive formulas for the confidence-weighted means and standard deviations from the summary statistics for individual records, we start with general formulas for the weighted arithmetic mean and unbiased weighted sample standard deviation in terms of the primary data $x_k$ and non-random weights $w_k$ (a.k.a "reliability weights" (Harrel et al., 2015) :

$$ {}_{w}AM = \sum_k w_k x_k \Big/ \sum_k w_k $$

$$ {}_{w}SD^2 = \frac{\sum_k w_k \left(x_k - wAM\right)^2}{\sum_k w_k - \left(\sum_k w_k^2 \Big/ \sum_k w_k\right)} $$

In our derivation of the confidence weighted statistics, we next group the primary data $x_k$ (which is seldom present in OEMD) by their record $i$, so that their $k$ indices are renumbered as follows:

| $i =$ | 1 | 2 | …. | $i$ | …. |
|---|---|---|---|---|---|
| $j =$ | 1, 2 … $N_1$ | 1, 2 … $N_2$ | …. | 1, 2 … $N_i$ | …. |

Since the same confidence weight $C_i$ for a given record $i$ is applied to all the primary data $x_{ij}$ in that record, the confidence weighted statistics are:

$$ \begin{aligned} {}_{cw}AM &= \sum_i C_i \sum_{j=1}^{N_i} x_{ij} \Big/ \sum_i \sum_{j=1}^{N_i} C_i \\ &= \sum_i C_i \sum_{j=1}^{N_i} x_{ij} \Big/ \sum_i C_i N_i \end{aligned} \tag{A17a} $$

$$ {}_{cw}SD^2 = \frac{\sum_i C_i \sum_{i=1}^{N_i} \left(x_{ij} - {}_{cw}AM\right)^2}{\sum_i C_i N_i - \left(\sum_i C_i^2 N_i \Big/ \sum_i C_i N_i\right)} \tag{A17b} $$

Now the summary statistics written in terms of the primary data are:

$$AM_i = \frac{1}{N_i}\sum_j x_{ij} \qquad \text{(A18a)}$$

$$SD_i^2 = \frac{\sum_{j=1}^{N_i}\left(x_{ij} - AM_j\right)^2}{N_i - 1} = \frac{\sum_j x_{ij}^2 - N_i AM_i^2}{N_i - 1} \qquad \text{(A18b)}$$

So they can be re-arranged as:

$$\sum_j x_{ij} = N_i AM_i \qquad \text{(A19a)}$$

$$\sum_j x_{ij}^2 = \left(N_i - 1\right) SD_i^2 + N_i AM_i^2 \qquad \text{(A19b)}$$

Now, eq. A19a can be substituted into eq. A17a in order to obtain the desired formula for the confidence weighted AM in terms of its component exposure AMs:

$${}_{cw}AM = \sum_i C_i N_i AM_i \Big/ \sum_i C_i N_i \qquad \text{(A20)}$$

To obtain the equivalent results for the confidence weighted SD, expand the numerator of eq. A17b:

$${}_{cw}SD^2 = \frac{\sum_{i,j} C_i {x_{ij}}^2 - 2\,{}_{cw}AM \sum_{i,j} C_i x_{ij} + {}_{cw}AM^2 \sum_i C_i N_i}{\sum_i C_i N_i - \left(\sum_i C_i^2 N_i \Big/ \sum_i C_i N_i\right)}$$

to get:

$${}_{cw}SD^2 = \frac{\sum_i C_i \sum_j {x_{ij}}^2 - {}_{cw}AM^2 \sum_i C_i N_i}{\sum_i C_i N_i - \left(\sum_i C_i^2 N_i \Big/ \sum_i C_i N_i\right)}$$

where eq. A19 was used.

Finally substitute eq. A18b to obtain the desired formula:

$$ {}_{cw}SD^2 = \frac{\sum_i C_i\left[\left(N_i-1\right)SD_i^2 + N_i\left(AM_i^2 - {}_{cw}AM^2\right)\right]}{\sum_i C_i N_i - \left(\sum_i C_i^2 N_i \Big/ \sum_i C_i N_i\right)} \tag{A21} $$

To obtain the confidence weighted geometric means and standard deviations, start with the log-transforms of eqs. A17 and A18:

$$ \ln {}_{cw}GM = \sum_{i,j} C_i y_{ij} \Big/ \sum_i C_i N_i $$

$$ \ln^2 {}_{cw}GSD = \frac{\sum_i C_i \sum_{i=1}^{N_i}\left(y_{ij} - \ln {}_{cw}GM\right)^2}{\sum_i C_i N_i - \left(\sum_i C_i^2 N_i \Big/ \sum_i C_i N_i\right)} $$

$$ \ln GM_i = \frac{1}{N_i}\sum_j y_{ij} $$

$$ \ln^2 \mathrm{GSD_i} = \frac{\sum_j \mathrm{y_{ij}^2} - \mathrm{N_i} \ln^2 \mathrm{GM_i}}{\mathrm{N_i} - 1} $$

where $y_{ij} = \ln x_{ij}$.

Following the same procedures as above, the desired formulas are quickly obtained:

$$ \ln {}_{cw}GM = \sum_i C_i N_i \ln GM_i \Big/ \sum_i C_i N_i \tag{A22} $$

$$ \ln^2 {}_{cw}GSD = \frac{\sum_i C_i\left[\left(N_i-1\right)\ln^2 GSD_i + N_i\left(\ln^2 GM_i - \ln^2 {}_{cw}GM\right)\right]}{\sum_i C_i N_i - \left(\sum_i C_i^2 N_i \Big/ \sum_i C_i N_i\right)} \tag{A23} $$

Q.E.D.

Finally, note that these pooling formulas (eqs. A20 – A23) can work correctly with OEMD records with a single measurement $x_i$ ($N_i = 1$) if their summary statistics are treated appropriately. From the definitions above of the arithmetic and geometric means, $x_i = AM_i = GM_i$ when $N_i = 1$. By making these substitutions for $N_i = 1$ records, eqs. A20 and A22 correctly calculate the confidence weighted means.

The values of the standard deviations for $N_i = 1$ records are arbitrary since their contributions to the pooling formulas (eqs. A21 and A23) are:

$$(N_i - 1)\, SD_i^2 = (N_i - 1) \ln^2 GSD_i = 0$$

For convenience in our SEM calculations, we set $SD_i = 0$ and $GSD_i = 1$ for $N_i = 1$ records, so they work correctly with the confidence-weighted variance formulas.

The degrees of freedom for the reliability-weighted variance (Harrel et al., 2015) is easily converted to the confidence-weighted degrees of freedom: ${}_{cw}df = \sum_i C_i N_i - \left( \sum_i C_i^2 N_i \Big/ \sum_i C_i N_i \right)$. Before ${}_{cw}df$ can be used to calculate 95% confidence limits on the confidence-weighted means, a comprehensive uncertainty measure should be derived by combining ${}_{cw}SD$ and ${}_{cw}GSD$ (representing the uncertainty from sample sizes $N_i$, the quality factors in $C_i$, and the within-source variability) with the uncertainties in our semi-empiric estimates of the summary means (Table 5).

## Bibliography

Aitchison J & Brown JAC. (1957) *The lognormal distribution.* Cambridge University Press: Cambridge, UK.

Bowman JD and Vila J. (2016) How Euclid's "mean proportional" became an estimation technique for modern scientists. Unpublished manuscript.

Bowman JD, Sivaganesan S, Shulman SA & Cardis E on behalf of the INTEROCC Study Group. (2013) Expert judgments of occupational exposures to electric and magnetic fields: I. A new method for evaluating the judgment's variability and uncertainty. Unpublished manuscript.

Harrell FE Jr, with contributions from Charles Dupont and many others. (2015). Hmisc: Harrell Miscellaneous. R package version 3.17-0. http://CRAN.R-project.org/package=Hmisc

Harter HL (1961). Expected values of normal order statistics. *Biometrika* 48: 151-165.

Ipsen J & Jerne NK. (1944). Graphical evaluation of the distribution of small experimental series. *Acta Pathologica Microbiologica Scandinavica*, 21: 343-361.

Royston JP. (1982) Algorithm AS 177: Expected normal order statistics (exact and approximate). *Journal of the Royal Statistical Society*. 31: 161-165.

Snedecor GW & Cochran WG. (1989) Normal probability plots. In: *Statistical Methods*. Iowa State University Press: Ames, USA, p. 59-60.

# 9. ALPHABETICAL INDEX

## 10. REFERENCES

Allen, S.G., Chadwick, P.J., Pearson, A.J., Whillock, M.J., Unsworth, C., Blackwell, R.P., Driscoll, C.M.H., 1994. Review of occupational exposure to optical radiation and electric and magnetic fields with regard to the proposed CEC physical agents directive. National Radiological Protection Board, Chilton, Didcot, Oxon.

Armstrong, B.G., 1998. Effect of measurement error on epidemiological studies of environmental and occupational exposures. Occup. Environ. Med. 55, 651–656.

Auger, C., 1998. Information sources in grey literature (guides to information sources). Bowker-Saur, London; New Providence, NJ.

Baan, R., Grosse, Y., Lauby-Secretan, B., El Ghissassi, F., Bouvard, V., Benbrahim-Tallaa, L., Guha, N., Islami, F., Galichet, L., Straif, K., 2011. Carcinogenicity of radiofrequency electromagnetic fields. Lancet Oncol. 12, 624–626.

Baste, V., Mild, K.H., Moen, B.E., 2010. Radiofrequency exposure on fast patrol boats in the Royal Norwegian Navy—an approach to a dose assessment. Bioelectromagnetics 31, 350–360. doi:10.1002/bem.20562

Bini, M., Checcucci, A., Ignesti, A., Millanta, L., Olmi, R., Rubino, N., Vanni, R., 1986. Exposure of workers to intense RF electric fields that leak from plastic sealers. J. Microw. Power Electromagn. Energy 21, 33–40.

Bitran, M.E., Charron, D.E., Nishio, J.M., 1992. Microwave emissions and operator exposure from traffic radars used in Ontario (No. 3189). Non Ionizing Radiation Section Radiation Protection Service Occupational Health & Saety Branch Ontario Ministry of Labour, Ontario, Canada.

Bondy, M.L., Scheurer, M.E., Malmer, B., Barnholtz-Sloan, J.S., Davis, F.G., Il’yasova, D., Kruchko, C., McCarthy, B.J., Rajaraman, P., Schwartzbaum, J.A., Sadetzki, S., Schlehofer, B., Tihan, T., Wiemels, J.L., Wrensch, M., Buffler, P.A., Brain Tumor Epidemiology Consortium, 2008. Brain tumor epidemiology: consensus from the Brain Tumor Epidemiology Consortium. Cancer 113, 1953–1968. doi:10.1002/cncr.23741

Bowman, J.D., Kincl, L., Shulman, S., Kelsh, M., Hansson Mild, K., van Tongeren, M., Yost, M., 2013. Expert Judgments of Occupational Exposures to Electric and Magnetic Fields: II. Job-Exposure Matrix for ELF Magnetic Fields. Ann. Occup. Hyg.

Bowman, J.D., Touchstone, J.A., Yost, M.G., 2007. A Population-Based Job Exposure Matrix for Power-Frequency Magnetic Fields. J. Occup. Environ. Hyg. 4, 715–728. doi:10.1080/15459620701528001

Bowman JD, 2014. Exposures to ELF-EMF in Everyday Environments, in: Röösli M. Epidemiology of Electromagnetic Fields, Barnes F, Greenebaum B. Biological Effects of Electromagnetics Series. CRC Press, Boca Raton, London, New York.

Bowman JD, Kelsh MA, Kaune WT, 1998. Manual for Measuring Occupational Electric and Magnetic Field Exposures. DHHS, CDC, National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio (USA).

Bradley, R., 1991. Traffic RADAR power densities: Summary of findings (No. IPTM Report). Institute of Police Technology and Management.

Burau, K.D., Huang, B., Whitehead, L.W., Delclos, G.M., Downs, T.D., 1998. A system linking occupation history questionnaire data and magnetic field monitoring data. J. Expo. Anal. Environ. Epidemiol. 8, 231–252.

Cardis, E., Richardson, L., Deltour, I., Armstrong, B., Feychting, M., Johansen, C., Kilkenny, M., McKinney, P., Modan, B., Sadetzki, S., Schüz, J., Swerdlow, A., Vrijheid, M., Auvinen, A., Berg, G., Blettner, M., Bowman, J., Brown, J., Chetrit, A., Christensen, H., Cook, A., Hepworth, S., Giles, G., Hours, M., Iavarone, I., Jarus-Hakak, A., Klaeboe, L., Krewski, D., Lagorio, S., Lönn, S., Mann, S., McBride, M., Muir, K., Nadon, L., Parent, M.-E., Pearce, N., Salminen, T., Schoemaker, M., Schlehofer, B., Siemiatycki, J., Taki, M., Takebayashi, T., Tynes, T., van Tongeren, M., Vecchia, P., Wiart, J., Woodward, A., Yamaguchi, N., 2007. The INTERPHONE study: design, epidemiological methods, and description of the study population. Eur. J. Epidemiol. 22, 647–664. doi:10.1007/s10654-007-9152-z

Chen, X.-L., Benkler, S., Chavannes, N., De Santis, V., Bakker, J., van Rhoon, G., Mosig, J., Kuster, N., 2013. Analysis of human brain exposure to low-frequency magnetic fields: a numerical assessment of spatially averaged electric fields and exposure limits. Bioelectromagnetics 34, 375–384. doi:10.1002/bem.21780

Cleveland, R.F., Sylvar, D.M., Ulcek, J.L., Mantiply, E.D., 1995. Measurement of Radiofrequency Fields and Potential Exposure from Land-Mobile Paging and Cellular Radio Base Station Antennas (Presentation), 17th Annual Meeting. Bioelectromagnetics Society. Bioelectromagnetics Society, Boston, MA (USA).

Coble, J.B., Dosemeci, M., Stewart, P.A., Blair, A., Bowman, J., Fine, H.A., Shapiro, W.R., Selker, R.G., Loeffler, J.S., Black, P.M., Linet, M.S., Inskip, P.D., 2009. Occupational exposure to magnetic fields and the risk of brain tumors. Neuro Oncol. 11, 242–249. doi:10.1215/15228517-2009-002

Conover, D.L., Moss, C.E., Murray, W.E., Edwards, R.M., Cox, C., Grajewski, B., Werren, D.M., Smith, J.M., 1992. Foot currents and ankle SARs induced by dielectric heaters. Bioelectromagnetics 13, 103–110. doi:10.1002/bem.2250130204

Cooper, T.G., 2002. Occupational exposure to electric and magnetic fields in the context of the ICNIRP guidelines (No. Report NRPB-W24). National Radiological Protection Board. HSE, UK.

Cooper, T.G., Allen, S.G., Blackwell, R.P., Litchfield, I., Mann, S.M., Pope, J.M., van Tongeren, M.J.A., 2004. Assessment of occupational exposure to radiofrequency fields and radiation. Radiat. Prot. Dosimetry 111, 191–203. doi:10.1093/rpd/nch334

Coureau, G., Bouvier, G., Lebailly, P., Fabbro-Peray, P., Gruber, A., Leffondre, K., Guillamo, J.-S., Loiseau, H., Mathoulin-Pélissier, S., Salamon, R., Baldi, I., 2014. Mobile phone use and brain tumours in the CERENAT case-control study. Occup. Environ. Med. 71, 514–522. doi:10.1136/oemed-2013-101754

Degrave, E., Meeusen, B., Grivegnée, A.-R., Boniol, M., Autier, P., 2009. Causes of death among Belgian professional military radar operators: a 37-year retrospective cohort study. Int. J. Cancer 124, 945–951. doi:10.1002/ijc.23988

Egger M, 2001. Systematic reviews in health care: meta-analysis in context. BMJ, London, UK.

Elder, R.L., Eure, J.A., Nicolls, J.W., 1974. Radiation Leakage Control of Industrial Microwave Power Devices. J. Microw. Power 9, 51–61.

European Parliament and Council, 2013. Directive 2013/35/ EU of the European Parliament and of the Council of 26 June 2013 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (electromagnetic fields) (20th individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) and repealing Directive 2004/40/EC.

Findlay, R.P., 2014. Induced electric fields in the MAXWEL surface-based human model from exposure to external low frequency electric fields. Radiat. Prot. Dosimetry 162, 244–253. doi:10.1093/rpd/nct281

Finkelstein, M.M., 1998. Cancer incidence among Ontario police officers. Am. J. Ind. Med. 34, 157–162.

Fisher, P.D., 1993. Microwave exposure levels encountered by police traffic radar operators. Electromagn. Compat. IEEE Trans. On 35, 36–45. doi:10.1109/15.249394

Floderus, B., Persson, T., Stenlund, C., Wennberg, A., Ost, A., Knave, B., 1993. Occupational exposure to electromagnetic fields in relation to leukemia and brain tumors: a case-control study in Sweden. Cancer Causes Control CCC 4, 465–476.

Floderus, B., Stenlund, C., Carlgren, F., 2002. Occupational exposures to high frequency electromagnetic fields in the intermediate range ( >300 Hz–10 MHz). Bioelectromagnetics 23, 568–577. doi:10.1002/bem.10050

Forssén, U.M., Mezei, G., Nise, G., Feychting, M., 2004. Occupational magnetic field exposure among women in Stockholm County, Sweden. Occup. Environ. Med. 61, 594–602.

Gobba, F., Bravo, G., Rossi, P., Contessa, G.M., Scaringi, M., 2011. Occupational and environmental exposure to extremely low frequency-magnetic fields: a personal monitoring study in a large group of workers in Italy. J. Expo. Sci. Environ. Epidemiol. 21, 634–645. doi:10.1038/jes.2011.9

Groves, F.D., Page, W.F., Gridley, G., Lisimaque, L., Stewart, P.A., Tarone, R.E., Gail, M.H., Boice, J.D., Beebe, G.W., 2002. Cancer in Korean war navy technicians: mortality survey after 40 years. Am. J. Epidemiol. 155, 810–818.

Håkansson, N., Floderus, B., Gustavsson, P., Johansen, C., Olsen, J.H., 2002. Cancer incidence and magnetic field exposure in industries using resistance welding in Sweden. Occup. Environ. Med. 59, 481–486.

Hardell, L., Carlberg, M., Söderqvist, F., Mild, K.H., 2013. Case-control study of the association between malignant brain tumours diagnosed between 2007 and 2009 and mobile and cordless phone use. Int. J. Oncol. 43, 1833–1845. doi:10.3892/ijo.2013.2111

Harrington, J.M., McBride, D.I., Sorahan, T., Paddle, G.M., van Tongeren, M., 1997. Occupational exposure to magnetic fields in relation to mortality from brain cancer among electricity generation and transmission workers. Occup. Environ. Med. 54, 7–13.

Hitchcock, R.T., Patterson, R.M., 1995. Radio-Frequency and ELF Electromagnetic Energies: A Handbook for Health Professionals. Van Nostrand Reinhold, New York.

Hitchcock, RT, 2015. Radio-Frequency Radiation, in: Hamilton and Hardy's Industrial Toxicology, Sixth Edition. John Wiley and Sons, Inc.

IARC, 2013. Non-ionizing radiation, Part 2: Radiofrequency electromagnetic fields. Int. Agency Res. Cancer Work. Group Eval. Carcinog. Risks Hum. 102, 1–460.

IARC, 2002. Non-ionizing radiation, Part 1: static and extremely low-frequency (ELF) electric and magnetic fields. Int. Agency Res. Cancer Work. Group Eval. Carcinog. Risks Hum. 80, 1–395.

ICNIRP, 2010. Guidelines for limiting exposure to time-varying electric and magnetic fields (1 Hz to 100 kHz). Health Phys., International Commission on Non-Ionizing Radiation Protection 99, 818–836. doi:10.1097/HP.0b013e3181f06c86

ICNIRP, 2009. Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz-300 GHz) - Review of the Scientific Evidence and Health Consequences.

ICNIRP, 1998a. Safety in the use of radiofrequency dielectric heaters and sealers: A practical guide.

ICNIRP, 1998b. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). International Commission on Non-Ionizing Radiation

Protection. Health Phys., International Commission on Non-Ionizing Radiation Protection 74, 494–522.

Joseph, W., Goeminne, F., Verloock, L., Vermeeren, G., Martens, L., 2012a. In situ occupational and general public exposure to VHF/UHF transmission for air traffic communication. Radiat. Prot. Dosimetry 151, 411–419. doi:10.1093/rpd/ncs016

Joseph, W., Vermeeren, G., Verloock, L., Goeminne, F., 2012b. In situ magnetic field exposure and ICNIRP-based safety distances for electronic article surveillance systems. Radiat. Prot. Dosimetry 148, 420–427. doi:10.1093/rpd/ncr206

Joyner, K.H., Bangay, M.J., 1986. Exposure Survey of Operators of Radiofrequency Dielectric Heaters in Australia. Health Phys. 50.

Juutilainen, J., Läärä, E., Pukkala, E., 1990. Incidence of leukaemia and brain tumours in Finnish workers exposed to ELF magnetic fields. Int. Arch. Occup. Environ. Health 62, 289–293.

Karipidis, K.K., Benke, G., Sim, M.R., Kauppinen, T., Giles, G., 2007. Occupational exposure to ionizing and non-ionizing radiation and risk of glioma. Occup. Med. Oxf. Engl. 57, 518–524. doi:10.1093/occmed/kqm078

Karipidis, K.K., Benke, G., Sim, M.R., Yost, M., Giles, G., 2007. Occupational exposure to low frequency magnetic fields and the risk of low grade and high grade glioma. Cancer Causes Control CCC 18, 305–313. doi:10.1007/s10552-006-0106-7

Kheifets, L., Bowman, J.D., Checkoway, H., Feychting, M., Harrington, J.M., Kavet, R., Marsh, G., Mezei, G., Renew, D.C., van Wijngaarden, E., 2009. Future needs of occupational epidemiology of extremely low frequency electric and magnetic fields: review and recommendations. Occup. Environ. Med. 66, 72–80. doi:10.1136/oem.2007.037994

Kheifets, L., Monroe, J., Vergara, X., Mezei, G., Afifi, A.A., 2008. Occupational electromagnetic fields and leukemia and brain cancer: an update to two meta-analyses. J. Occup. Environ. Med. Am. Coll. Occup. Environ. Med. 50, 677–688. doi:10.1097/JOM.0b013e3181757a27

Kheifets, L.I., 2001. Electric and magnetic field exposure and brain cancer: a review. Bioelectromagnetics Suppl 5, S120-131.

Kheifets, L.I., Afifi, A.A., Buffler, P.A., Zhang, Z.W., 1995. Occupational electric and magnetic field exposure and brain cancer: a meta-analysis. J. Occup. Environ. Med. Am. Coll. Occup. Environ. Med. 37, 1327–1341.

Koeman, T., van den Brandt, P.A., Slottje, P., Schouten, L.J., Goldbohm, R.A., Kromhout, H., Vermeulen, R., 2014. Occupational extremely low-frequency magnetic field exposure and selected cancer outcomes in a prospective Dutch cohort. Cancer Causes Control CCC 25, 203–214. doi:10.1007/s10552-013-0322-x

Koh, D.-H., Locke, S.J., Chen, Y.-C., Purdue, M.P., Friesen, M.C., 2015. Lead exposure in US worksites: A literature review and development of an occupational lead exposure database from the published literature. Am. J. Ind. Med. 58, 605–616. doi:10.1002/ajim.22448

Kromhout, H., Symanski, E., Rappaport, S.M., 1993. A comprehensive evaluation of within- and between-worker components of occupational exposure to chemical agents. Ann. Occup. Hyg. 37, 253–270.

Lagorio, S., Rossi, S., Vecchia, P., De Santis, M., Bastianini, L., Fusilli, M., Ferrucci, A., Desideri, E., Comba, P., 1997. Mortality of plastic-ware workers exposed to radiofrequencies. Bioelectromagnetics 18, 418–421.

Lagunas-Solar, M.C., Zeng, N.X., Essert, T.K., Truong, T.D., Cecilia Piña, U., 2006. Radiofrequency power disinfects and disinfests food, soils and wastewater. Calif. Agric. 60, 192–199. doi:10.3733/ca.v060n04p192

Lambdin, D.L., EPA, U.S., 1979. An investigation of energy densities in the vicinity of vehicles with mobile communications equipment and near a hand-held walkie talkie, Technical note - Office of Radiation Programs ; ORP/EAD 79-2. Environmental Protection Agency, Office of Radiation Programs, Electromagnetic Radiation Analysis Branch, Las Vegas, Nev. (USA).

Lavoué, J., Bégin, D., Beaudry, C., Gérin, M., 2007. Monte Carlo simulation to reconstruct formaldehyde exposure levels from summary parameters reported in the literature. Ann. Occup. Hyg. 51, 161–172. doi:10.1093/annhyg/mel068

Light, R., Pillemer, D., 1984. Summing up: the science of reviewing research. Harvard University Press, Cambridge, Mass., USA.

Lilienfeld, A., 1978. Foreign service health status study: evaluation of health status of foreign service and other employees from selected Eastern European posts : final report. Dept. of Epidemiology, School of Hygiene and Public Health, Johns Hopkins University, Baltimore, Md.

Liljestrand, B., Sandström, M., Hansson Mild, K., 2003. RF Exposure During Use of Electrosurgical Units. Electromagn. Biol. Med. 22, 127–132. doi:10.1081/JBC-120024622

Loomis, D.P., Savitz, D.A., 1990. Mortality from brain cancer and leukaemia among electrical workers. Br. J. Ind. Med. 47, 633–638.

Lotz, W.G., Rinsky, R.A., Edwards, R.D., 1995. Occupational Exposure of Police Officers to Microwave Radiation from Traffic Radar Device (No. NTIS Publication Number PB95-261350). National Institute for Occupational Safety and Health, Cincinnati, Ohio (USA).

Mann, S., 2011. Exposure Assessment for Epidemiological Studies. International Scientific Conference on Electromagnetic Fields & Public Health. Oral presentation. Brussels, Belgium. Accessed: 2016-09-16. Available at: http://ec.europa.eu/health/electromagnetic_fields/docs/ev_20111116_co05_en.pdf.

Mann, S., 2010. Assessing personal exposures to environmental radiofrequency electromagnetic fields. Physique 11, 541–555.

Mann S, Addison DS, Blackwell RP, Khalid M, 2005. Personal Dosimetry of RF Radiation - Laboratory and Volunteer Trials of an RF Personal Exposure Meter, HPA-RPD Series Reports.

Mantiply, E.D., Pohl, K.R., Poppell, S.W., Murphy, J.A., 1997. Summary of measured radiofrequency electric and magnetic fields (10 kHz to 30 GHz) in the general and work environment. Bioelectromagnetics 18, 563–577. doi:10.1002/(SICI)1521-186X(1997)18:8<563::AID-BEM5>3.0.CO;2-0

Milham, S., 1988. Mortality by license class in amateur radio operators. Am. J. Epidemiol. 128, 1175–1176.

Morgan, R.W., Kelsh, M.A., Zhao, K., Exuzides, K.A., Heringer, S., Negrete, W., 2000. Radiofrequency exposure and mortality from cancer of the brain and lymphatic/hematopoietic systems. Epidemiol. Camb. Mass 11, 118–127.

Mueller, C.H., Krueger, H., Schierz, C., 2002. Project NEMESIS: perception of a 50 Hz electric and magnetic field at low intensities (laboratory experiment). Bioelectromagnetics 23, 26–36.

Murata, Taichi K, 2015. Modeling Military Exposures to RF Electric Fields for the INTEROCC Study.

Navas-Acién, A., Pollán, M., Gustavsson, P., Plato, N., 2002. Occupation, exposure to chemicals and risk of gliomas and meningiomas in Sweden. Am. J. Ind. Med. 42, 214–227. doi:10.1002/ajim.10107

Ostrom, Q.T., Bauchet, L., Davis, F.G., Deltour, I., Fisher, J.L., Langer, C.E., Pekmezci, M., Schwartzbaum, J.A., Turner, M.C., Walsh, K.M., Wrensch, M.R., Barnholtz-Sloan, J.S., 2014. The epidemiology of glioma in adults: a “state of the science” review. Neuro-Oncol. 16, 896–913. doi:10.1093/neuonc/nou087

Peak, D.W., 1975. Measurement of power density from marine radar. U.S. Dept. of Health, Education, and Welfare, Public Health Service, Food and Drug Administration, Bureau of Radiological Health, Rockville, Md. : Washington.

Pfetzing E, Allen B, 1994. Guidelines for Statistical Analysis of Occupational Exposure Data (No. EPA-68-D2-0064). US Environmental Protection Agency (USEPA), Washington, DC.

Rappaport, S.M., Lyles, R.H., Kupper, L.L., 1995. An exposure-assessments strategy accounting for within- and between-worker sources of variability. Ann. Occup. Hyg. 39, 469–495.

Repacholi, M.H., 1981. Sources and Applications of Radiofrequency (RF) and Microwave Energy, in: Grandolfo, M., Michaelson, S.M., Rindi, A. (Eds.), Biological Effects and Dosimetry of Nonionizing Radiation. Springer US, pp. 19–41.

Robinette, C.D., Silverman, C., Jablon, S., 1980. Effects upon health of occupational exposure to microwave radiation (radar). Am. J. Epidemiol. 112, 39–53.

Rodvall, Y., Ahlbom, A., Stenlund, C., Preston-Martin, S., Lindh, T., Spännare, B., 1998. Occupational exposure to magnetic fields and brain tumours in central Sweden. Eur. J. Epidemiol. 14, 563–569.

Röösli M, 2014. Epidemiology of Electromagnetic Fields [WWW Document]. CRC Press. URL https://www.crcpress.com/Epidemiology-of-

Electromagnetic-Fields/Roosli/p/book/9781466568167 (accessed 9.10.16).

Ruggera, P.S., 1979. Measurements of electromagnetic fields in the close proximity of CB antennas (No. HEW Publication (FDA) 79-8080). Final Report Bureau of Radiological Health, Div. of Electronic Products, Rockville, MD (USA).

Sadetzki, S., Langer, C.E., Bruchim, R., Kundi, M., Merletti, F., Vermeulen, R., Kromhout, H., Lee, A.-K., Maslanyj, M., Sim, M.R., Taki, M., Wiart, J., Armstrong, B., Milne, E., Benke, G., Schattner, R., Hutter, H.-P., Woehrer, A., Krewski, D., Mohipp, C., Momoli, F., Ritvo, P., Spinelli, J., Lacour, B., Delmas, D., Remen, T., Radon, K., Weinmann, T., Klostermann, S., Heinrich, S., Petridou, E., Bouka, E., Panagopoulou, P., Dikshit, R., Nagrani, R., Even-Nir, H., Chetrit, A., Maule, M., Migliore, E., Filippini, G., Miligi, L., Mattioli, S., Yamaguchi, N., Kojimahara, N., Ha, M., Choi, K.-H., Mannetje, A. ’t, Eng, A., Woodward, A., Carretero, G., Alguacil, J., Aragones, N., Suare-Varela, M.M., Goedhart, G., Schouten-van Meeteren, A.A.Y.N., Reedijk, A.A.M.J., Cardis, E., 2014. The MOBI-Kids Study Protocol: Challenges in Assessing Childhood and Adolescent Exposure to Electromagnetic Fields from Wireless Telecommunication Technologies and Possible Association with Brain Tumor Risk. Front. Public Health 2, 124. doi:10.3389/fpubh.2014.00124

Savitz, D.A., Cai, J., van Wijngaarden, E., Loomis, D., Mihlan, G., Dufort, V., Kleckner, R.C., Nylander-French, L., Kromhout, H., Zhou, H., 2000. Case-cohort analysis of brain cancer and leukemia in electric utility workers using a refined magnetic field job-exposure matrix. Am. J. Ind. Med. 38, 417–425.

Savitz, D.A., Loomis, D.P., 1995. Magnetic field exposure in relation to leukemia and brain cancer mortality among electric utility workers. Am. J. Epidemiol. 141, 123–134.

Schüz, J., Elliott, P., Auvinen, A., Kromhout, H., Poulsen, A.H., Johansen, C., Olsen, J.H., Hillert, L., Feychting, M., Fremling, K., Toledano, M., Heinävaara, S., Slottje, P., Vermeulen, R., Ahlbom, A., 2011. An international prospective cohort study of mobile phone users and health (Cosmos): design considerations and enrolment. Cancer Epidemiol. 35, 37–43. doi:10.1016/j.canep.2010.08.001

Sienkiewicz Z, Schüz J, Poulsen AH, Cardis E, 2012. EFHRAN Report on Risk analysis of human exposure to electromagnetic fields (revised). Deliverable Report D2, European Health Risk Assessment Network on Electromagnetic Fields Exposure.

Skotte, J., 1984. Exposure of radio officers to radio frequency radiation on Danish merchant ships. Am. Ind. Hyg. Assoc. J. 45, 791–795.

Sorahan, T., Nichols, L., van Tongeren, M., Harrington, J.M., 2001. Occupational exposure to magnetic fields relative to mortality from brain tumours: updated and revised findings from a study of United Kingdom electricity generation and transmission workers, 1973-97. Occup. Environ. Med. 58, 626–630.

Speers, M.A., Dobbins, J.G., Miller, V.S., 1988. Occupational exposures and brain cancer mortality: a preliminary study of east Texas residents. Am. J. Ind. Med. 13, 629–638.

Stam, R., 2014. The revised electromagnetic fields directive and worker exposure in environments with high magnetic flux densities. Ann. Occup. Hyg. 58, 529–541. doi:10.1093/annhyg/meu010

Stuchly, M.A., Repacholi, M.H., Lecuyer, D., Mann, R., 1980. Radiation survey of dielectric (RF) heaters in Canada. J. Microw. Power 15, 113–121.

Szmigielski, S., 1996. Cancer morbidity in subjects occupationally exposed to high frequency (radiofrequency and microwave) electromagnetic radiation. Sci. Total Environ. 180, 9–17.

Tell, R.A., Hankin, N.M., Janes, D.E., 1976. Aircraft Radar Measurements in the Near Field, Proceedings of the Ninth Midyear Topical Symposium of Health Physics Society. Denver, Colorado.

Tell, R.A., Nelson, J.C., 1974. RF Pulse Spectral Measurements in the Vicinity of Several Air Traffic Control Radars (No. Report # EPA-520/1-74-005). US Environmental Protection Agency. Office of Radiation Programs.

Tielemans, E., Marquart, H., De Cock, J., Groenewold, M., Van Hemmen, J., 2002. A proposal for evaluation of exposure data. Ann. Occup. Hyg. 46, 287–297.

Turner, M.C., Benke, G., Bowman, J.D., Figuerola, J., Fleming, S., Hours, M., Kincl, L., Krewski, D., McLean, D., Parent, M.-E., Richardson, L., Sadetzki, S., Schlaefer, K., Schlehofer, B., Schuz, J., Siemiatycki, J., Van Tongeren, M., Cardis, E., 2014. Occupational exposure to extremely low frequency magnetic fields and brain tumour risks in the INTEROCC study. Cancer Epidemiol. Biomarkers Prev. doi:10.1158/1055-9965.EPI-14-0102

Tynes, T., Hannevik, M., Andersen, A., Vistnes, A., Haldorsen, T., 1996. Incidence of breast cancer in Norwegian female radio and telegraph operators. Cancer Causes Control 7, 197–204. doi:http://dx.doi.org/10.1007/BF00051295

Tynes, T., Jynge, H., Vistnes, A.I., 1994. Leukemia and brain tumors in Norwegian railway workers, a nested case-control study. Am. J. Epidemiol. 139, 645–653.

Ungers, L.J., Mihlan, G.J., Jones, J.H., 1984. In-depth survey report: control technology for microelectronics industry at Xerox Corporation, Microelectronics Center, El Segundo, California (No. Report CT-115-12b). National Institute for Occupational Safety and Health.

Van Den Bossche, M., Verloock, L., Aerts, S., Joseph, W., Martens, L., 2015. In situ exposure assessment of intermediate frequency fields of diverse devices. Radiat. Prot. Dosimetry 164, 252–264. doi:10.1093/rpd/ncu257

Vila, J., 2016. Exposure meta-analysis: a methodology for collecting, assessing and summarizing exposure measurement data from the literature. Prep.

Vila, J., Bowman, J.D., Figuerola, J., Morina, D., Kincl, L., Richardson, L., Cardis, E., on behalf of the INTEROCC Study Group, 2016a. Development of a source-exposure matrix for occupational exposure assessment of electromagnetic fields in the INTEROCC study. J Expo Sci Env. Epidemiol In press.

Vila, J., Bowman, J.D., Richardson, L., Kincl, L., Conover, D.L., McLean, D., Mann, S., Vecchia, P., van Tongeren, M., Cardis, E., INTEROCC Study Group, 2016b. A Source-based Measurement Database for Occupational Exposure Assessment of Electromagnetic Fields in the INTEROCC Study: A Literature Review Approach. Ann. Occup. Hyg. 60, 184–204. doi:10.1093/annhyg/mev076

Villeneuve, P.J., Agnew, D.A., Johnson, K.C., Mao, Y., Canadian Cancer Registries Epidemiology Research Group, 2002. Brain cancer and occupational exposure to magnetic fields among men: results from a Canadian population-based case-control study. Int. J. Epidemiol. 31, 210–217.

Wertheimer, N., Leeper, E., 1979. Electrical wiring configurations and childhood cancer. Am. J. Epidemiol. 109, 273–284.

Wilén, J., Hörnsten, R., Sandström, M., Bjerle, P., Wiklund, U., Stensson, O., Lyskov, E., Mild, K.H., 2004. Electromagnetic field exposure and health among RF plastic sealer operators. Bioelectromagnetics 25, 5–15. doi:10.1002/bem.10154

Wyde, M., Cesta, M., Blystone, C., Elmore, S., Foster, P., Hooth, M., Kissling, G., Malarkey, D., Sills, R., Stout, M., Walker, N., Witt, K., Wolfe, M., Bucher, J., 2016. Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposure). bioRxiv. doi:10.1101/055699