

**PUBLICATIONS OF  
THE UNIVERSITY OF EASTERN FINLAND**

*Dissertations in Forestry and  
Natural Sciences*



UNIVERSITY OF  
EASTERN FINLAND

**TUOMO ESKELINEN**

**LOW FREQUENCY MAGNETIC FIELDS:  
EXPOSURE ASSESSMENT AND REPRODUCTIVE RISKS**



**TUOMO ESKELINEN**

*Low frequency magnetic  
fields: exposure assessment  
and reproductive risks*

Publications of the University of Eastern Finland  
Dissertations in Forestry and Natural Sciences  
No 224

Academic Dissertation

To be presented by permission of the Faculty of Science and Forestry for public  
examination in the Auditorium Sn201 in Snellmania Building at the University of  
Eastern Finland, Kuopio, on 2<sup>nd</sup> of June, 2016, at 12 o'clock noon.  
Department of Environmental and Biological Sciences

Grano Oy  
Jyväskylä, 2016  
Editor: Research Dir. Pertti Pasanen

Distribution:  
University of Eastern Finland Library / Sales of publications  
P.O.Box 107, FI-80101 Joensuu, Finland  
tel. +358-50-3058396  
[www.uef.fi/kirjasto](http://www.uef.fi/kirjasto)

ISBN: 978-952-61-2139-0 (Print)

ISBN: 978-952-61-2140-6 (PDF)

ISSNL: 1798-5668

ISSN: 1798-5668

ISSN: 1798-5676 (PDF)

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# *Abstract*

Exposure to low frequency magnetic fields (LF MFs) in our homes, at work, at schools, and at transport is common nowadays. There are many ubiquitous sources of extremely low frequency (ELF; frequencies below 300 Hz) MFs, e.g. electrical power lines, cables and appliances. In recent years, equipment such as induction hobs and electronic article surveillance equipment, have become more common which has increased human exposure to intermediate frequency (IF; 300 Hz-10 MHz) MFs. At the same time, there is a lack of information on the possible health risks of these exposures. The complexity and wide range of frequencies and sources mean that undertaking a truly representative MF exposure assessment is very challenging.

One problem in epidemiological studies into health risks has been insufficient understanding of the validity of the methods that have been used to characterize MF exposure of the study subjects, a crucial aspect of these kinds of studies. Complete characterization of exposure is generally not feasible, and approximate methods may introduce considerable exposure measurement errors that may bias the risk estimates.

The aims of this study were to assess residential and occupational exposures to LF MFs, to evaluate the validity of short-term measurements as exposure assessment methods in epidemiological studies, and to assess the possible association of ELF MF exposures with adverse reproductive outcomes.

Short-term MF measurements were found to be a useful method to assess exposure in an epidemiological study. Spot measurements carried out in all rooms of a sample of apartments were correlated with 24-h personal exposure, and the average of the spot measurements of a residence was found to be the best way to summarize the spot measurements, resulting in smallest exposure measurement error. It was also noted that spot measurements performed about equally well in

predicting 24-h average MF exposure and time spent above a given magnetic field strength.

The person making spot measurements also wore a recording MF meter during the 20-min visits to the residences. The 20-min measurement was found to provide some information about the temporal variability of MFs, and it can be used for assessing 24-h average exposure. However, it did not offer any advantages compared to the spot measurements.

An epidemiological study was conducted to investigate the association of ELF MF exposure with reproductive outcomes. Exposure was assessed by both a questionnaire and the short-term measurements validated in the above-described studies. Neither time to pregnancy, birth weight nor small-for-gestational age of the newborn was associated with ELF MF exposure. High ELF MF exposures were rare, which was a limitation of the study.

Measurements of the occupational exposure of cashiers identified them as a group of workers exposed to IF MFs and therefore as a suitable group for epidemiological studies on possible health effects of IF MFs. The measurements also provided data that can be used for IF MF exposure assessment in an epidemiological study.

*National Library of Medicine Classification: QT 140, QT 162.M3, WA 470*

*Medical Subject Headings: Magnetic Fields; Environmental Exposure; Occupational Exposure; Epidemiological Studies; Validation Studies as Topic; Reproduction/radiation effects*



## TIIVISTELMÄ

Altistuminen pientaajuisille magneettikentille on yleistä kodeissa, kouluissa, työpaikoilla ja liikenteessä. Esimerkiksi sähkölinjat ja -kaapelit, sekä erilaiset sähkölaitteet ovat yleisiä hyvin pientaajuisten (alle 300 Hz) magneettikenttien lähteitä. Viime vuosina yleistyneet sähkölaitteet, kuten induktioliedet ja varashälytinlaitteet, ovat lisänneet altistumista välitaajuisille (300 Hz-10 MHz) magneettikentille. Magneettikenttäaltistumisten mahdollisista terveysvaikutuksista tiedetään tällä hetkellä vähän. Terveysvaikutusten arvioimiseksi tarvitaan luotettavaa altistumistietoa. Altistumisen arviointi on kuitenkin hyvin haasteellista mm. siksi että magneettikenttien lähteitä ja taajuuksia on paljon, eikä tiedetä mikä tai mitkä altistumista kuvaavat parametrit ovat yhteydessä terveysvaikutuksiin.

Yksi terveysvaikutustutkimusten ongelma on riittämätön tieto altistumisen arviointimenetelmien validiteetista eli siitä, kuinka hyvin käytetty menetelmä antaa tietoa tutkittavien henkilöiden todellisesta altistumisesta. Virhe altistumisen arvioinnissa voi vääristää arvioita terveysriskin suuruudesta.

Tutkimuksen tavoitteena oli arvioida asuin- ja työympäristössä tapahtuvaa altistumista hyvin pientaajuisille ja välitaajuisille magneettikentille. Validiteettitutkimuksissa tavoitteena oli arvioida, kuinka hyvin pientaajuisten magneettikentän lyhytaikaismittaukset soveltuvat altistumisen arviointiin epidemiologisissa tutkimuksissa. Lisäksi selvitettiin hyvin pientaajuisten magneettikenttien mahdollisia haitallisia vaikutuksia lisääntymisterveyteen.

Lyhytaikaismittauksien havaittiin olevan käyttökelpoinen menetelmä arvioitaessa hyvin pientaajuisille magneettikentille altistumista epidemiologisissa tutkimuksissa. Pistemittaukset, joita tehtiin asunnon kaikissa huoneissa, korreloivat 24 tunnin henkilökohtaisen altistumisen kanssa. Lisäksi havaittiin, että huoneiston pistemittausten keskiarvo oli paras tapa tiivistää pistemittauksista saatava tieto siten että altistumismittauksen

virhe olisi mahdollisimman pieni. Pistemittaukset olivat yhtä hyviä ennustamaan sekä 24 tunnin keskimääräistä magneettikenttäaltistumista että altistumisaikaa tietyn kynnyksarvon ylittävälle magneettikentälle.

Pistemittaukset huoneistoissa tehnyt henkilö piti mukanaan tallentavaa magneettikenttämittaria 20 minuutin mittauskynnin aikana. Tämän 20 minuutin mittauksen havaittiin tuottavan hieman tietoa magneettikentän vaihtelevuudesta, ja sen havaittiin olevan käyttökelpoinen arvioitaessa keskimääräistä 24 tunnin altistumista. Menetelmä ei kuitenkaan ole parempi kuin pistemittaukset.

Epidemiologisessa tutkimuksessa selvitettiin hyvin pientaajuisille magneettikentille altistumisen mahdollista yhteyttä lisääntymisterveyteen. Altistumisen arviointi perustui kyselyihin ja lyhytaikaismittauksiin, jotka oli validoitu edellä kuvatuissa tutkimuksissa. Raskauden viiveen, lapsen syntymäpainon ja raskausviikkoihin suhteutetun pienipainoisuuden ei havaittu olevan yhteydessä altistumiseen hyvin pientaajuisille magneettikentille. Tulosten tulkintaa kuitenkin rajoittaa korkeiden magneettikenttäaltistumisten pieni osuus.

Kassatyöntekijät havaittiin mittauksissa työntekijäryhmäksi, joka altistuu välitaajuisille magneettikentille, ja siksi soveltuu hyvin kohderyhmäksi välitaajuuskenttien terveysvaikutustutkimuksiin. Mittaustuloksia voidaan hyödyntää tutkimushenkilöiden altistumisluokitteluun tulevissa epidemiologisissa tutkimuksissa.

*Avainsanat: magneettikentät; altistuminen; epidemiologia; validiteetti; lisääntyminen; lisääntymisterveys*

# *Preface*

This study was carried out at the Department of Environmental and Biological Sciences, University of Eastern Finland (previously University of Kuopio) during the years 1998-2003, and 2015-2016. The work was financially supported by the Imatran Voima Foundation and the Finnish Work Environment Fund, and I am thankful for this support.

I am sincerely grateful to my principal supervisor, Professor Jukka Juutilainen. First of all, he offered me the opportunity to start with my doctoral studies. He provided me excellent guidance, and had a major role in the designing of all studies. I sincerely thank my other supervisor, Dr. Päivi Roivainen for her valuable advice and great comments during the preparation of the thesis. Besides scientific expertise and thinking, I thank the opportunity of sharing an innovative, idea-rich and enthusiastic atmosphere.

I wish to thank the official pre-examiners, Professor Martin Rööslä and Associate Professor Roel Vermeulen. I am also grateful to Ewen MacDonald, Pharm.D for revising the language and style of the thesis.

When I began working in the Department of Environmental Sciences, the epidemiological study was already started by Mr. Jari Keinänen. I thank Jari for the hard work he has done to collect data. I also thank Mr. Juha Niiranen and Assistant Professor Heidi Salonen as well as Mr. Teemu Toivonen for their contribution in data acquisition.

The Radiation Research Group was my home team during this study. A big hand to each member of this team: Dr. Jonne Naarala, Dr. Ari Markkanen, Dr. Anne Höytö, Ms. Hanne Säppi, Dr. Päivi Heikkinen, Dr. Timo Kumlin, Dr. Sakari Lang, Dr. Jukka Luukkonen, and Professor emeritus Tapio Rytömaa. This group represents exceptional knowledge and talent on radiation research, and it has been pleasant to be a part of the team. I also thank all

the staff at the Department of Environmental and Biological Sciences.

I thank Dr. Kari Jokela from STUK for his valuable help and expertise on novel MF measurements. I thank Dr. Seppo Saarikoski and Mr. Olavi Kauhanen from Kuopio University Hospital –they made the registry information available for the epidemiological study. I also appreciate the help and comments to the epidemiological study from Dr. Pia Verkasalo from THL and Dr. Markku Sallmen from FIOH. I also thank Dr. Timo Kauppinen from FIOH for his advice on aspects of occupational exposure assessment.

Mr. Per-Johan Hagelberg from Checkpoint-Meto and Mr. Juha Teirilä from SOK are acknowledged for making the occupational exposure measurements in stores possible.

I thank Savonia University of Applied Sciences and my colleagues for support. Especially Mr. Pentti Mäkelä, who worked in FIOH when this study started, played a remarkable role as an expert in statistical tools and methods, and this contribution is highly appreciated. I also warmly thank two of my colleagues, Ms. Anja Kainulainen and Dr. Miika Kajanus for their interest in my research.

I thank my family and parents Ulla and Veikko – both of you had an important and unique role when making this research. My mother was very supportive during the years. I also thank warmly my brothers Terho, Jouni and Jouko, and sister Henna and their families. Jouko contributed to some MF measurements which were used in this thesis. Aino and Hannu –thank you for encouragement.

I thank a number of friends, family members and relatives for your kind support. I thank Jari and Jaana for encouragement.

Annika, Tommi, Peggy, Tomas –you have been in my thoughts many times when making this study. Obviously I hope that the youngest people are the ones who would benefit from the results. This thesis is dedicated to you. I am also most grateful to Marjo for her warm support.

Tuomo Eskelinen



## LIST OF ABBREVIATIONS

ANOVA	Analysis of variance
B	Magnetic flux density
B <sub>peak</sub>	Peak (maximum) value
CI	Confidence interval
ELF	Extremely low frequency
EMF	Electric and magnetic fields or Electromagnetic fields;
G	Unit for magnetic flux density (B), 1 m(milli)G =0.1 μ(micro)T
H	A vector quantity which specifies an MF at any point in space, and is expressed in ampere per meter (A/ m)
HCC	High current configuration
ICNIRP	International Commission for Non-Ionizing Radiation Protection
IEEE	Institute of Electrical and Electronics Engineers
IF	Intermediate frequency
IUGR	Intrauterine growth retardation (In practice =SGA, SFD) )
LBW	Low birth weight
LCC	Low current configuration
MF	Magnetic field
NTD	Neural tube defect
OR	Odds ratio
RCM	Rate of change
RR	Relative risk
SD	Standard deviation
SES	Socioeconomic status
SGA, SFD	Small-for-gestational age, Small-for-date
T	Tesla, unit for magnetic flux density (B)
TWA	Time weighted average
VDT, VDU	Visual display terminal, Visual display unit
VLF	Very low frequency

## LIST OF DEFINITIONS

<b>Confounding</b>	Spurious findings due to the effect of a variable that is correlated with both the exposure and disease under study.
<b>Congenital</b>	Inborn
<b>Exposure metric</b>	A single number that summarizes an electric and/or magnetic field exposure over a period of time.
<b>Fetus, Foetus</b>	The stage of prenatal development between the embryo and birth.
<b>Frequency</b>	The number of cycles completed by electromagnetic waves in 1 s; usually expressed in hertz (Hz)
<b>Frequency response</b>	An instrument's output as a function of frequency relative to the magnitude of the input signal. Specification of an instrument's frequency response includes the type of filter and its bandwidth
<b>Gestational age</b>	Age of foetus from the beginning date of last menstruation
<b>Magnetic field</b>	A vector quantity, H, specifies an MF at any point in space, and is expressed in ampere per meter (A/ m)
<b>Magnetic flux density</b>	Intensity of magnetic field in Tesla (T)
<b>Misclassification</b>	Measurement error in categorical variables
<b>Prenatal</b>	Before birth
<b>Primigravida</b>	A woman who is pregnant for the first time (is defined as a "nullipara" during pregnancy)
<b>Primipara</b>	A woman who is giving birth for the first time
<b>Sensitivity</b>	The sensitivity of the exposure measure is the proportion of those who truly have the exposure who will be correctly classified as exposed
<b>Spesificity</b>	The proportion of those who are truly unexposed who will be classified as unexposed
<b>Small-for-gestational age, Small-for-date</b>	A newborn whose birth weight is less than the birth weight of about 90% of foetuses of the same gestational age

## **LIST OF ORIGINAL PUBLICATIONS**

This thesis is based on data presented in the following articles, referred to by the Roman numerals I–IV.

- I** Eskelinen T, Keinänen J, Salonen H, Juutilainen J. 2002. Use of spot measurements for assessing residential ELF magnetic field exposure: a validity study. *Bioelectromagnetics* 23:173-176.
  
- II** Eskelinen T, Niiranen J, Juutilainen J. 2003. Use of short-term measurements for assessing temporal variability of residential ELF magnetic field exposure. *Journal of Exposure Analysis and Environmental Epidemiology* 13:372-377.
  
- III** Eskelinen T, Roivainen P, Mäkelä P, Keinänen J, Kauhanen O, Saarikoski S, Juutilainen J. Maternal exposure to extremely low frequency magnetic fields: association with time to pregnancy and foetal growth. Submitted.
  
- IV** Roivainen P, Eskelinen T, Jokela K, Juutilainen J. 2014. Occupational exposure to intermediate frequency and extremely low frequency magnetic fields among personnel working near electronic article surveillance systems. *Bioelectromagnetics* 35:245-250.

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## **AUTHOR'S CONTRIBUTION**

- Study I      The studies were planned by all authors. Jari Keinänen and Heidi Salonen performed the practical measurements, and the author, together with Jukka Juutilainen, conducted the analysis. The author wrote the first draft of the manuscript and all co-authors contributed to the subsequent writing process.
- Study II     The studies were planned by all authors. Juha Niiranen performed the practical measurements, and the author together with Jukka Juutilainen made the analysis. The author wrote the first draft of the manuscript and all co-authors contributed to the subsequent writing process.
- Study III    The study was planned by Jukka Juutilainen, Olavi Kauhanen and Seppo Saarikoski. Jari Keinänen performed the measurements. The author collected and prepared the data for statistical analysis. The author and Pentti Mäkelä conducted the statistical analyses and all authors contributed to interpretation of results. The author wrote the first draft of the manuscript in collaboration with Päivi Roivainen. All authors contributed to the subsequent writing process.
- Study IV    The study was planned by the author and Jukka Juutilainen. The author conducted the measurements and analyzed the results. The first draft of the manuscript was written by Päivi Roivainen, and all co-authors contributed to the subsequent writing process.



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# *1. General Introduction*

## **1.1 ELECTROMAGNETIC FIELDS AND THEIR HEALTH EFFECTS**

### **1.1.1 Electromagnetic fields**

Electric and magnetic fields (EMFs) are present when electricity is generated, transmitted or distributed in power lines or cables, or when using electrical appliances. Time-varying EMFs are produced by alternating currents. Electric fields (EFs) are created by differences in voltage: the higher the voltage, the stronger will be the resultant field. Magnetic fields (MFs) develop when an electric current flows: the greater the current, the stronger the MF. Like EFs, MFs are strongest close to their origin and rapidly decrease at greater distances from the source. MFs are not blocked by common materials such as the walls of buildings (WHO, 1999).

International Commission for Non-Ionizing Radiation Protection (ICNIRP) defines extremely low frequency (ELF) EMFs as having a frequency below 300 Hz, and intermediate frequency (IF) EMFs having a frequency range from 300 Hz to 30 MHz, between those of ELF and radiofrequency (RF) (ICNIRP, 1998). World Health Organization (WHO) defines IF from 300 Hz to 10 MHz (WHO, 2007a). The electromagnetic spectrum and some typical sources of EMFs are presented in Table 1.

This thesis focuses on low frequency (ELF and IF) MFs. At low frequencies, there is more evidence that it is the MFs rather than EFs that exert adverse health effects (WHO, 2007ab).

**Table 1.** *The electromagnetic spectrum.*

<i>Non-ionising radiation</i>				<i>Ionising radiation</i>	
Static field	Extremely low frequency	Intermediate frequency	Radio frequency	Optical radiation (ultraviolet, visible light, infrared)	X-rays, gamma rays
0 Hz	> 0 – 300 Hz	> 300 Hz – 10 Mhz	> 10 MHz – 300 GHz	> 300 GHz – 3 PHz	
Magnetic resonance imaging	Power lines, household appliances	Induction hobs, anti-theft & security systems,	TV, FM, radio transmitters, cellular phones, antitheft & security systems	Lamps, lasers	Radioactive sources

The intensity of MF can be specified in two ways - as magnetic flux density, B, in tesla (T), or as MF strength, H, in amperes per meter (A/m). The two quantities are related by the expression:

$$B = \mu H \quad (1)$$

where  $\mu$  is the constant of proportionality (the magnetic permeability). In a vacuum and air, as well as in non-magnetic (including biological) materials,  $\mu$  has the value  $4 \times 10^{-7}$ , in Henry per meter (H/m) (ICNIRP, 2010).

### 1.1.2 Exposure to low frequency magnetic fields

Potential sources of exposure to ELF MFs are equipment that include conductors carrying electric current, e.g. electric motors, installations such as electric power lines, and appliances in residences. Residential exposures are dominated by ELF sources but also include sources of radio and microwave frequencies (NIEHS, 1998).

Residential exposures of ELF MF in homes do not vary very extensively (NIEHS, 1998; WHO, 2007ab). Besides distance to the source, factors affecting exposure are type and age of dwelling, floor of dwelling, and season. Higher values are typical in urban/semi

urban residences versus rural areas (Calvente et al., 2014). In the Electric Power Research Institute (EPRI) '1000 homes study' the overall average spot magnitude of the MF inside the surveyed residences was  $0.09 \mu\text{T}$  (Zaffanella, 1993). The median value for the average spot MF was  $0.06 \mu\text{T}$  and exceeded  $0.29$  in 5% of all measured residences. In Austria, the median values of night-time ELF MFs at 50 Hz decreased from  $0.014$  to  $0.011 \mu\text{T}$  in measurements repeated in 113 residences in 2006, 2009, and 2012 (Tomitsch and Dechant, 2012, 2015). However, in a location close to power lines, MFs can reach approximately  $20 \mu\text{T}$ , and EFs can be between several hundreds and several thousands of volts per meter (WHO, 2007ab).

A Finnish study reported MFs of  $0.098 - 2.1 \mu\text{T}$  near external sources and in reference residences as  $0.066-0.080 \mu\text{T}$  (Juutilainen et al., 1989). Ilonen et al. (2008) also examined the field levels in Finnish buildings; the apartment mean of spot measurements was  $0.62 \mu\text{T}$  in apartments above an indoor transformer station,  $0.21 \mu\text{T}$  in the first floor reference apartments, and  $0.11 \mu\text{T}$  in the upper floor reference apartments. The 24-h apartment mean was  $0.56 \mu\text{T}$  in apartments above a transformer station,  $0.21 \mu\text{T}$  in the first floor reference apartments, and  $0.10 \mu\text{T}$  in the upper floor reference apartments.

There is an increasing number of MF sources of human exposure in the IF frequency range (SCENIHR, 2015). These sources include induction, electrical processing equipment, radio-broadcasting, video display units, anti-theft detection and intelligent labelling devices as well as equipment used for non-destructive testing and in medicine. More appliances have appeared in the IF range also in domestic households. For example, induction hobs can expose their users (both members of the general public and professionals) to IF MFs higher than the reference levels of exposure guidelines (SCENIHR, 2015). ELF and IF-MF exposures were characterized in one study in the dwellings of children of the Spanish Childhood-"INMA" population-based birth cohort (Calvente et al., 2014). Reference levels set by ICNIRP were not exceeded but there were large differences between homes in terms of the mean and maximum values. Overall, there is little data available on the residential IF-MF exposure.

The magnitude and distribution of EMF exposures from appliances are not well known (WHO, 2007a). There are several factors that contribute to exposure by appliances e.g. type of appliance, its age, its distance from the person using it, and the pattern and duration of use. Exposure to MFs from appliances tends to be short-term and intermittent (WHO, 2007a). A study conducted by Mader & Peralta (1992) indicated that appliances are not a significant source of whole-body exposure, but they may be the dominant source of exposure for the extremities. Close to some appliances, the instantaneous MF values can be as high as few hundreds of  $\mu\text{T}$ . Computers and cellular phones may contribute appreciably to total daily exposure. In the study of Mezei et al. (2001), computers contributed appreciably to the overall exposure while other appliances each contributed less than 2%. In another study, common domestic electrical appliances were responsible for an exposure comparable to that from power lines (Delpizzo, 1990).

Increased exposures are possible in transport, where the frequencies can be lower (e.g. 25 or 16.7 Hz from electrified railroad lines) in addition to 50 or 60 Hz from other sources (Wenzl, 1997). In hybrid cars, MFs of 0.06–0.09  $\mu\text{T}$  have been measured: on the back seat, 16-69% of measurements displayed levels higher than 0.2  $\mu\text{T}$  (Hareuveny et al., 2015). Furthermore, school buildings may be located near to power lines, which can contribute to indoor EMF. Potential exposure sources in schools are large transformers, and other EMF-generating equipment inside the buildings similar to large office complexes and industrial settings (NIEHS, 1998).

Occupational exposures occur by and large at 50/60 Hz frequencies and their harmonics (WHO, 2007a). Conductors carrying high currents can cause exposures approximately as high as 10 mT. In occupations involving electricity, the average MF exposures have ranged from 0.4–0.6  $\mu\text{T}$  for electricians and electrical engineers, and were approximately 1.0  $\mu\text{T}$  for power line workers. Welders, railway engine drivers and sewing machine operators experience the highest MF exposures (above 3  $\mu\text{T}$ ) (WHO, 2007a). In electric sub-stations, MF levels up to 50  $\mu\text{T}$  have been reported (Hosseini et al., 2015).

New sources of low frequency MF exposure include solar photovoltaic generation facilities. These facilities are the sites where



the current generated by the solar panels is converted into three-phase 50 /60 Hz power that is fed into the grid. The highest ELF MFs have been measured close to transformers and inverters, and RF fields from 5 to 100 kHz close to inverters (Tell et al., 2015). The low frequency MFs complied with IEEE (2002), and ICNIRP (2010) occupational exposure limits.

Exposures to ELF MF levels higher than 0.4  $\mu\text{T}$  have been measured for dentists (Huang et al., 2011). In uninterruptible power supply workplaces (Tesneli and Tesneli, 2014) and in sites adjacent to 110 kV gas-insulated substations (GIS) (Korpinen and Pääkkönen, 2015), the values of ELF MF did not exceed the low or high action levels of the Directive 2013/35/EU. Inside the GISs, MF values varied from 0.4 to 43.0  $\mu\text{T}$ , and EFs from 5 to 90 V m<sup>(-1)</sup>. In the cable room of GIS, the maximum value very near to the cables was 250  $\mu\text{T}$ .

### **1.1.3 Health effects of low frequency magnetic fields**

#### **1.1.3.1 Acute effects and exposure guidelines**

High exposures to LF fields can affect the nervous system of human beings. In addition, exposure to ELF EFs induces a surface electric charge which can lead to micro-shocks, or other non-hazardous effects (WHO, 2007a).

Exposure limits based on the acute effects on electrically excitable tissues, particularly those on the central nervous system, have been proposed by international organizations (ICNIRP, 1998; IEEE, 2002; ICNIRP, 2010). The low frequency (LF) part of the ICNIRP (1998) guidelines was replaced in 2010 by revised guidelines (ICNIRP, 2010). In 2013, the European Commission published a Directive on the minimum health and safety requirements regarding exposure of workers to the risks arising from physical agents (Directive 2013/35/EU). The Directive includes physical quantities regarding exposure to EMFs, exposure limit values and action levels in the IF frequency range, and exposure limit values and action levels based on thermal effects in the frequency range from 100 kHz to 300 GHz. The values are based on the ICNIRP guidelines. Some examples of the reference levels (ICNIRP, 2010) and action levels (EU, 2013) are

presented in Table 2. The frequencies (other than 50 Hz) shown in Table 2 are typical for antitheft devices.

**Table 2.** *Examples of reference levels (ICNIRP, 2010) and Low/High action levels (AL) (EU, 2013) for selected frequencies of exposure to time-varying magnetic fields.*

Frequency	ICNIRP General public, $\mu\text{T}$ (RMS)	ICNIRP Occupational, $\mu\text{T}$ (RMS)	Low AL, $\mu\text{T}$ (RMS)	High AL, $\mu\text{T}$ (RMS)
50 Hz	200	1000	1000	6000
5 kHz	27	100	100	100
7.5 kHz	27	100	100	100
58 kHz	27	100	100	100

### 1.1.3.2 Chronic effects

A health risk assessment also needs to consider chronic low-intensity exposure. Epidemiological studies have shown a rather consistent pattern of increased risk for childhood leukaemia associated with 50-60 Hz MFs above 0.3-0.4  $\mu\text{T}$  (Ziegelberger et al., 2011). The evidence is not strong enough to be considered causal, but sufficiently convincing to remain a concern. International Agency for Research on Cancer has classified ELF MFs as “possibly carcinogenic to humans (Class 2B) (IARC, 2002). The absence of established causality means that this effect cannot be addressed in the basic restrictions (ICNIRP, 2010), but risk management advice with precautionary measures has been offered (WHO, 2007ab). Assuming that the association is causal, on a worldwide scale, the best point estimates range from 100 to 2400 yearly childhood leukaemia cases attributable to ELF MF exposure (Kheifets et al., 2006). These estimates represent from 0.2% to 4.9% of the total annual number of childhood leukaemia cases, which has been estimated to be around 49 000 worldwide in 2000 (IARC, 2000). These estimations are very imprecise and they are highly dependent

on unverified assumptions about the exposure prevalence and distribution and on the effect of exposure on the disease (WHO, 2007a).

Many diseases have been investigated for their possible association with ELF MF exposure i.e. cancers in both children and adults, depression, suicide, reproductive dysfunction, developmental disorders, immunological modifications and neurological diseases (WHO, 2007a). The scientific evidence supporting the link between ELF MFs and any of these diseases is weaker than for childhood leukaemia but strongest for an association between ELF MF exposure and Alzheimer's disease, (e.g. García et al., 2008; Vergara et al., 2013), For some health outcomes, such as cardiovascular disease or breast cancer, the evidence is sufficient to state with confidence that ELF MFs do not cause the disease (WHO, 2007a).

While ELF and radiofrequency MFs have been targeted in many studies, only a very limited number of studies have addressed the exposure to and health effects of IF EMFs (Juutilainen & Eskelinen 1999; Litvak et al., 2002; SCENIHR 2015).

## **1.2 LOW FREQUENCY MAGNETIC FIELDS EXPOSURE ASSESSMENT IN EPIDEMIOLOGICAL STUDIES**

### **1.2.1 Exposure measurement error and misclassification**

In epidemiological studies, exposure assessment methods range from objective methods or measurements to techniques that depend on the subjective ability of study subjects to recall information (White et al., 2008). Measurement error is a major source of bias; it can potentially lead to spurious conclusions about the relationship between exposure and disease. Measurement error of exposure has been defined as the difference between the measured exposure and the true exposure (Armstrong et al., 1995; White et al., 2008).

For example, the measurement error can be caused by erroneous design or usage of the instrument, errors in the data collection protocol, or errors in recalling past exposure. Furthermore, differences in biological characteristics, or errors in data entry and analysis can cause a measurement error (Armstrong et al., 1995; White et al., 2008).

In the case of retrospective exposure data, which is common in epidemiological studies, a differential exposure measurement error is a major concern (Armstrong et al., 1995). This occurs when the exposure measurement error differs according to the disease or outcome under study. Recall bias can be a reason for differential measurement error; this occurs when cases report exposure differently from controls. This differential exposure measurement error can lead to a bias in the estimation of the odds ratio, or in some other measure of association between the exposure and outcome, which is called a misclassification bias or information bias.

Exposure measurement error is referred to as misclassification, when exposure measurement involves the subdivision of study subjects into two or more exposure levels. In the case of a dichotomous exposure classification, sensitivity and specificity is often used to describe the level of misclassification (e.g. Lamina et al., 2008; Quédrego et al., 2013; Carter et al., 2015). The sensitivity of an exposure measure is the proportion of truly exposed subjects who are correctly classified as exposed. The specificity of an

exposure measure is the proportion of truly unexposed subjects who are correctly classified as unexposed (Armstrong et al., 1995).

### 1.2.2 Measurements of low frequency magnetic field

Exposure measurements are used to classify attributes of subjects or environmental agents relevant to their health, with the assignment of numerals (or other signs to these classes). The exposure variables used are continuous, ordered categorical, nominal categorical, or dichotomous (Armstrong et al., 1995).

In most studies on LF magnetic fields, the root mean square (rms) value of magnetic flux density (B) is measured. For a pure sinusoidal waveform, the rms magnetic flux density value is related to the instantaneous peak value by a factor of  $\sqrt{2}$ , i.e.  $B_{\text{peak}} = \sqrt{2}B_{\text{rms}}$  (NIEHS 1998; ICNIRP 1998; ICNIRP 2010).

The MF meters usually record the magnitude of the MF without information on the directional orientation in space or changes in direction over time. This is accomplished by measuring the rms value of three orthogonal spatial components (x, y, and z), and then combining these three values to determine the total magnitude (resultant) of the MF, which is computed as follows:

$$B_{\text{res}} = \sqrt{B_x^2 + B_y^2 + B_z^2} \quad (2)$$

where  $B_x$ ,  $B_y$  and  $B_z$  are the orthogonal magnetic flux density spatial components.

The challenge for exposure assessment of LF MFs is to choose a summary measure that is both physically meaningful and biologically relevant (NIEHS, 1998). Since the critical exposure parameters for biological effects are not known, it is recommended to evaluate alternative exposure metrics (Juutilainen et al., 1996; Schoenfeld et al., 1999; Neutra and Delpizzo, 2001). Time-weighted average (TWA) MF (or the product of MF strength and time) has been used in most epidemiological studies. However, there are many alternative metrics which have been proposed, for example, time within an exposure range, field intermittency (rate of change),

field stability, and maximum MF (Morgan et al., 1995; Villeneuve et al., 1998; Schoenfeld et al., 1999; van der Woord et al., 1999; Hansen et al., 2000; Schüz et al., 2000; McDevitt et al., 2002).

Many different exposure metrics have also been used in epidemiological studies, including arithmetic mean, geometric mean, median (50th percentile), peak (maximum) value, 99th percentile, percent of time above a threshold, percent of time in a field strength window, total harmonic distortion, high frequency electric transients, rate of change, standardized rate of change, standard deviation, and MF “dose” defined as the product of MF strength and time (Zaffanella 1993, Armstrong 1995, Juutilainen et al., 1996; NIEHS 1998, Hansen et al., 2000; Auvinen et al., 2000; Foliart et al., 2001; Levallois et al., 2001; Li et al., 2001; Lee et al., 2002; Li et al., 2002;; Lewis et al., 2015). Although some studies have reported associations between alternative exposure metrics (other than the average MF) and the health endpoint studied, no consistent pattern has emerged. It has also been pointed out that studies using TWA as a metric have found elevated risks, and that any other metric must be sufficiently correlated with TWA, in order to explain the observed associations (WHO, 2007a).

In the case of pulsed and broadband fields, two alternative ways to assess exposure have been presented. The first alternative to analyze exposure to non-sinusoidal MFs below 100 kHz is based on a spectral comparison of each component to the corresponding reference level (ICNIRP, 2010). In the second alternative, the waveform of B or dB/dt is filtered in the time domain with a simple filter, where the attenuation varies proportionally to the reference level as a function of frequency, and the filtered peak value is compared to the peak reference level derived from the ICNIRP reference levels (Jokela, 2007).

### **1.2.2.1 Spot measurements**

Spot measurement can be defined as a reading made at a point in time in one single place (Armstrong et al., 1995). In attempts to capture spatial variations of field, some studies have made multiple spot measurements at different places, eg., in or around the home.

For example, Juutilainen et al. (1989, 1993) conducted MF measurements inside apartments in the kitchen, bedroom, and living room. In each room, a five-point method was applied where one measurement was taken in the center of the room, and the other four measurements made at 1.4 meter from each corner, at one meter height. In the bedroom, the center measurement was taken on the top of the center of the bed, and then the average (arithmetic mean) was calculated for each room and for the whole residence. The major drawback of spot measurements is their inability to capture temporal variations. As with all measurements, spot measurements can assess only contemporary exposure. Thus, spot measurements provide only an approximation even for the contemporary field, because of short-term temporal variations in the fields. Seasonal variations can be taken into account by repeating the measurements throughout the year. It has been stated that basically they are not useful in the assessment of historical exposure, which is an intrinsic requirement for retrospective studies. (WHO, 2007a). However, spot measurements have been used in many retrospective studies as a proxy measure of study subjects past exposure (e.g. Juutilainen et al., 1993; Vergara et al., 2015b).

Results have been published on the validity of short-term measurements for estimating long-term time-average exposure (Delpizzo et al., 1991; Delpizzo and Salzberg, 1992; Kaune et al., 1994; Kaune and Zaffanella, 1994; Schüz et al., 2000, Rankin et al., 2002), but little is known about the usability of short-term measurements for estimating other exposure metrics. However, one study reported that residential point-in-time spot measurements can be used (in addition to time-average MF) to estimate time spent above a MF threshold (Juutilainen et al., 1996).

#### **1.2.2.2 Longer term MF measurements**

Many studies (e.g. Juutilainen et al., 1989; Tomitch et al, 2010; Tomitch and Dechant 2012, 2015; Calvente et al., 2014; Karipidis 2015) have performed longer term measurements of MF at one or more locations. Normally the duration of measurements has been 24–48h, but also longer measurement times (e.g. 7 days) have been used (Lewis et al., 2015). One group of investigators repeated their

measurements in different years in the same residences (Tomitsch and Dechant, 2012 and 2015). Comparisons of measurements have found poor-to-fair agreement between long-term and short-term measurements (Schüz et al., 2000).

In recent studies in residential environments, spot measurements have been used together with 24-h measurements, which have been conducted in bedroom or rooms where children spend most of their time (Ilonen et al., 2008; Karipidis 2015; Vergara et al., 2015b).

### **1.2.2.3 Personal exposure monitoring**

In personal exposure monitoring, the study subject wears a meter on the body which captures exposure to fields from all sources and at all places. Because all sources are included, the average fields measured tend to be higher than those derived from spot or long-term measurements. Personal exposure monitoring represents one way to validate other types of measurements or estimates. However, a differential exposure misclassification is possible; this has been associated to the use of personal exposure monitoring in case-control studies where age- or disease-related changes in behavior affect personal measurement (WHO, 2007a).

### **1.2.3 Other exposure assessment methods**

#### **1.2.3.1 Wire codes**

The Wertheimer-Leeper (W-L) wire code (for example, HCC = high current configuration and LCC = low current configuration) is a construct that has been used as a surrogate indicator of residential exposure to MFs in some epidemiological studies (Wertheimer & Leeper 1982; Leeper et al. 1991; Tworeger et al., 2002). Wire codes have been mostly used in North American studies, as their applicability is limited in other countries, where power connections to homes are mostly underground (WHO, 2007ab). There is no consensus on whether the concept of wire coding is a feasible crude surrogate with reports in support (e.g. Tarone et al., 1998; O’Leary et al., 2003), but others claiming that it is an imperfect surrogate for



the assessment of MF exposure in a variety of environments (Tworeger, 2002; WHO, 2007a). The study of O'Leary et al. (2003) found minimal bias due to misclassification of wire code categories, similar to the result by Tarone et al. (1998). On the other hand, Tworeger et al. (2002) reported that misclassification masked the shape of a threshold (nonlinear) dose-response curve and changed the slope of a linear dose-response curve. It is evident that any misclassification of exposure over time may change the estimation of the odds ratios and mask possible dose-response relationships.

Kheifets et al. (1997) concluded that wire codes explain rather little of the variance of measured residential MFs, (e.g. 16% according to Savitz et al., 1988 and <21% according to Rankin et al., 2002), but they may still be useful in identifying homes with potentially high MFs.

### **1.2.3.2 Distance from power lines and other sources**

Distance from power lines has been widely used as a MF exposure surrogate in epidemiological studies (e.g. Olsen et al., 1993; Draper et al., 2005; Auger et al., 2010, 2012; Pedersen et al.; 2014; deVocht et al., 2014; de Vocht and Lee, 2014). The basic idea is to devise a cut-off distance which divides the study subjects into exposed and unexposed. MF intensity decreases with distance from power lines. Several study-specific cut-off distances have been used, for example Draper et al. (2005) and Pedersen et al. (2014), estimated relative risk of leukaemia by comparing children who lived > 600 m distance from a power line at birth, with children who lived within 200 m, and those who were born between 200 and 600 m from a power line compared to children who lived within 200 m.

The drawback of using distance is that exposures from other sources can cause a misclassification of exposure, when, e.g. distance to power lines is used as the only method to assess exposure of the study subjects. This approach neglects other residential MF sources in the apartments and the dependency on distance is not identical for different MF sources (different sizes of power lines, sub-stations etc.), resulting in a large exposure

measurement error. Furthermore, if one uses long cut-off distances (such as 200 m), this inevitably results in the inclusion of a high number of subjects whose exposure does not differ from the normal residential background. Overall, distance is known to be poor predictor of magnetic field exposure (WHO, 2007a).

### **1.2.3.3 Exposure assessment based on indoor transformers**

Indoor transformers in residential buildings provide a novel approach to investigate possible adverse health effects of ELF MFs. Exposure to ELF MF can be assessed based on the location of apartments in relation to the transformer: residents of apartments adjacent to the indoor transformer are exposed to elevated MFs while the exposure in other apartments of the same building is at normal residential background level. The results of Ilonen et al. (2008) indicated that apartments can be reliably classified into high and low MF categories based on the known location of transformer stations. This conclusion was based on extensive MF measurements in the apartments above transformer stations, and in reference apartments in the same buildings. Spot measurements conducted in all rooms (five measurements per room) and 24-h measurements were used to estimate the 24-h average MF level of each residence. Further studies showed that data on the structural characteristics of transformers provided valuable information about exposure levels and are potentially useful for evaluating the exposure-response relationship (Okokon et al., 2014). Huss et al. (2013) also have suggested that the classification of individuals into 'high' and 'low' exposure categories is possible based on the location of their apartment within a building with an indoor transformer, and that this categorization could be applied in epidemiological studies. Similar results have been obtained in many other studies (e.g. Thuróczy et al., 2008; Rööslí et al., 2011,). Classification of exposure based on location of transformers has not yet been used in epidemiological studies. The potential benefit of this method is that it is possible to identify study subjects who are being subjected to relatively high exposures of ELF MF. However, also

misclassification of exposure is possible, for example, due to other sources of exposure, or variabilities in the MF in different parts of the residence.

#### **1.2.3.4 Calculated historical fields**

Calculated historical fields from transmission lines in homes have been used in some epidemiological cancer studies (Feychting & Ahlbom, 1993, 1994; Olsen et al., 1993; Valjus et al., 1995; Feychting et al., 1996; Li et al., 1997; Vergara et al., 2015b), and also as part of residential planning (Zaffanella et al., 1997). Feychting & Ahlbom (1993) evaluated the model by comparing calculations based on contemporary transmission line currents with contemporary spot measurements. In single-dwelling homes, the calculated and measured MFs showed a good agreement. For example, in the highest measurement category ( $>0.2 \mu\text{T}$ ), only 15% of the calculations underestimated the contemporary measurements.

Bowman et al. (1999) studied residential MFs calculated in residences using a physically based multipole model. The predictions were better correlated with the bedroom readings ( $R=0.4$ ) than with Wertheimer-Leeper wire codes ( $R=0.27$ ).

Vergara et al. (2015b) reported good correlation between calculated fields and spot measurements of fields taken on site during visits to the residences. These findings have been interpreted to mean that one can achieve high specificity in an exposure assessment, which is essential for examining the association between MFs from power lines and health outcome.

#### **1.2.3.5 Questionnaires and exposure assessment from appliances**

A self-administered questionnaire is a tool designed to gather and record recalled exposure from subjects in an epidemiological study. It contains questions to be answered by the subject, or possible options from which the subject chooses those which are appropriate to him or her. A questionnaire design should help to obtain estimates of exposure variables with minimum measurement error,

and to create an instrument which is easy for the interviewer and subject to use, and for the investigator to process and analyze (Armstrong et al., 1995). Questionnaires are sensitive to recall error, such as poor recall or low impact exposures and their main advantage is their inexpensive cost (White et al., 2008). In addition to recall bias, questionnaires can also be answered by other household members. This can be an advantage (e.g. to obtain a higher response rate), but it may also introduce an additional source of error.

In epidemiological studies on ELF MFs, questionnaires have been frequently used for the assessment of appliance use. However, it is not known how well data from questionnaires correspond to the actual exposure (Mills et al., 2000). Mezei et al. (2001) reported that questionnaire-based information on appliance use, even when focused on use within the last year, had very limited value in estimating personal exposure to MFs. According to Behrens et al. (2004), interview-based exposure information (on the use of RF-emitting appliances) can result in misclassification and biased risk estimates.

An appropriate method for combining assessments of exposure from different appliances and chronic exposure from other sources would inevitably be dependent on assumptions made about exposure metrics, and such methods need to be developed (WHO, 2007a).

#### **1.2.3.6 Job titles and job exposure matrix**

A job-exposure matrix (JEM) is a tool which can be used to assess exposure to potential health hazards in occupational epidemiological studies.

A JEM comprises a list of levels of exposure to a variety of harmful (or potentially harmful) agents for selected occupational titles. In large population-based epidemiological studies, JEMs may be used as a quick and systematic means of converting coded occupational data (job titles) into a matrix of possible exposures, obviating the need to assess each individual's exposure in detail. (Kauppinen et al., 1992). A JEM usually contains cross-tabulated classified exposure information subdivided by agent and

occupational class. It can also contain definitions, inferences, exposure data, and references, which enables the use as a general exposure information system for hazard control, risk quantification and hazard surveillance (Kauppinen et al., 1998).

Early versions of JEMs can be traced back to the 1940s, but the first modern JEM was reported in 1980 (Hoar et al., 1980; NIEHS, 1998). JEMs have proved to be useful in the elucidation of a true association between exposure to 50-Hz MF and disease (Johansen et al., 2002). However, if the observed risk estimates are small, potential biases need to be considered. For example, electrical shocks or other unidentified variables associated with occupations where employees work with electrical equipment, rather than the MF exposure, may be responsible for the observed associations with disease (Li et al., 2009).

Job titles with presumed elevated EMF exposure and JEM have been widely used in epidemiological studies to evaluate occupational MF exposures, for example to study the risk of myocardial infarction (Ahlbom et al., 2004), brain cancer and leukaemia (Savitz et al., 2000; Li et al., 2009), amyotrophic lateral sclerosis (Zhou et al., 2012) or effects of parental occupational exposure to 50 Hz MFs (Blaasaas et al., 2002). Job and industry title can be used as surrogates for exposure to EMF because they allow assumptions to be made about the workers' duties – some tasks can be associated with elevated or low exposure to EMF (NIEHS, 1998). Nonetheless, retrospective exposure assessment from job titles can pose problems, since workers with the same job title or workers in the same industry today may not have the same exposure as employees doing the same job 20-30 years ago. Furthermore, some job titles may have disappeared when technologies have changed (NIEHS, 1998).

It has been proposed that more complete JEMs should be developed, combining job title, work environment and task, and an index of exposure to EMFs, spark discharges, contact currents, and other chemical and physical agents (Kheifets et al., 2009). A JEM of electric shocks exposure for 501 job titles has been established (Vergara et al., 2015a).

### **1.3 EPIDEMIOLOGICAL STUDIES ON REPRODUCTIVE RISKS RELATED TO LOW FREQUENCY MAGNETIC FIELDS**

Epidemiological studies on maternal and paternal ELF MF exposures and pregnancy outcomes are presented in Table 3. These studies have investigated miscarriages, birth weight development, and small for gestational age of newborn, congenital abnormalities, preterm birth and stillbirth.

The first part of Table 3 collates the studies on LF MFs and miscarriages. Most of the 14 studies have used questionnaires and personal interviews in the assessment of MF exposure, although many studies have also included MF measurements. In a few studies, wire codes were used to assess exposure, whereas proximity to MF sources was used in two recent studies (Auger et al., 2010, 2012). In two studies, combined exposure assessment methods have been applied (Juutilainen et al., 1993; Mahram et al., 2013). Personal exposure measurements were used in the studies of Li et al., (2001) and Lee et al., (2002).

A risk of miscarriage has been associated with ELF MF exposure (Lindbohm et al., 1992, Li et al., 2002, Lee et al., 2002). One of the most comprehensive studies from the exposure assessment point of view was conducted by Lindbohm et al. (1992). They made a retrospective study of miscarriages among bank clerks and clerical workers using video display terminals (VDTs) during 1975-85. Job histories, VDT use, reproductive risk factors, and ergonomic factors were enquired in the questionnaires. Exposure to MFs from VDTs was assessed from the questionnaires, company records on the VDT models used by different work groups, and laboratory measurements of IF and ELF MFs at a fixed location (in order to approximate the proximity to the foetus) near to the various VDT models. An increased risk was reported in association with exposure to ELF MFs from VDTs, expressed both as rms magnitude  $>0.24 \mu\text{T}$  and cumulative exposure per week; the increase was statistically significant for the highest exposure category. In addition, there were indications of exposure-response relationships, which were not further analyzed. Exposure to IF fields (about 20

kHz; very low exposure level) from the VDTs was not associated with any increased risk.

In contrast to the findings of Lindbohm et al. (1992), a number of studies have detected no association between adverse pregnancy outcomes and use of VDTs (Kurppa et al., 1985; Ericson and Källén, 1986; Goldhaber et al., 1988; McDonald et al., 1988; Bryant and Love, 1989; Brandt and Nielsen, 1990; Windham et al., 1990; Schnorr et al., 1991; Nielsen and Brandt, 1992). In these studies, exposure to MFs from VDTs was assessed based on self-reporting questionnaires and interviews by phone or interviews made in the hospital. The ELF and IF MF emissions of VDTs are generally weak, and since these studies did not include any measurements to identify those VDTs with high MFs, they are not very informative.

Slight increases in the risk estimates for miscarriage have been observed for the use of electric blankets during pregnancy (Wertheimer and Leeper, 1986; Belanger et al., 1998), but also decreased risks have been reported (Lee et al., 2000).

Measurement-based studies have provided limited evidence for an increased miscarriage risk associated with residential ELF MF exposure (Juutilainen et al., 1993; Lee et al., 2002; Li et al., 2002; Wang et al., 2013). Details of these studies are described below.

An increased risk of early pregnancy loss (pre-clinical miscarriage) has been associated with residential MF exposure of 0.6  $\mu\text{T}$  or higher (Juutilainen et al., 1993). In that study, MF spot measurements were taken at the front door of the residences of all participants. Measurements inside the residences were made in 48% of the cases and in 57% of control residences. Occupational MF exposure was assessed on the basis of job classification and measurements. The main analysis was conducted based on the front door measurements, as these were available for all subjects. When the analysis was based on exposure in three categories, an elevated OR was observed for the highest exposure group ( $\geq 0.63 \mu\text{T}$ ) versus the lowest ( $< 0.13 \mu\text{T}$ ), but the intermediate exposure group did not have a higher risk than the lowest exposure group.

Li et al. (2002) observed no significant association of miscarriage with TWA MF exposure, but a significantly increased risk was found when the exposure metric used was maximum exposure above 1.6  $\mu\text{T}$ . The association was stronger among women whose

measurement (by body-worn meter) had been taken during a “typical day”. This result has been explained and discussed as a reflection of lower exposure misclassification among these study subjects (Savitz, 2002; McKinlay et al., 2004; Mezei et al., 2006). It has been postulated that the magnitude of the maximum, but not the 95th or 99th percentile, is affected by the sampling rate of the meter and the mobility of the wearer (Mezei et al., 2006). The case-control study conducted by Lee et al. (2002) observed statistically significant associations and dose response trends with increasing exposure quartiles, for maximum exposure and rate-of-change of the MF, but TWA was not significantly associated with the risk of suffering a miscarriage. The MF exposure was assessed by personal exposure measurements. A prospective sub-study of 219 subjects produced consistent results (Lee et al., 2002). In addition to an increased miscarriage risk associated with high rate-of-change and maximum field values, also the personal TWA exposure at home (but not total 24-h TWA exposure) showed a statistically significantly increased risk for fields above 0.2  $\mu$ T.

Wang et al. (2013) observed a positive association between residential maximum MF exposure and miscarriage, but the associations between different MF exposure metrics and miscarriage were not consistent. Exposure to MF was estimated by measurements at the front doors and in the alley in front of the subjects' homes. No significantly increased risk of miscarriage was found to be associated with the average front-door exposure, but a significant association with maximum alley exposure was detected ( $p=0.001$ ). The validity of the MF measurements as estimates of personal exposure is not known, which precludes drawing any definitive conclusions.

There is little evidence of increased risks of adverse pregnancy outcomes other than miscarriage (WHO, 2007a). The second part of Table 3 lists the studies on birth weight (BW) and small for gestational age (SGA) associated with ELF MF exposure. In these studies, questionnaires and interviews were the most frequently used methods for assessing MF exposure. Proximity to the MF source has been used in four recent studies (Auger, 2010; Mahram et al., 2013; de Vocht et al., 2014; de Vocht and Lee, 2014). The third



part of Table 3 includes studies on LF MF and other possible reproductive outcomes.

Bracken et al. (1995) assessed residential sources of ELF MF, such as electrically heated beds and wire codes, but also occupational exposures, by seven-day monitoring of MFs and questionnaires on VDT use. The study subjects' personal exposure was measured with the AMEX-2 wrist monitor and furthermore occupational exposures were also assessed. The outcomes, low birth weight (LBW) (<2500 g) and intrauterine growth retardation were not associated with VDT use or TWA exposure to MFs. MFs were measured with the one direction field sensor (AMEX-2), which produces less accurate measures than can be obtained with three-axis monitors. Grajewski et al. (1997) did not observe any increased risk of reduced BW and preterm birth associated with occupational VDT exposure estimated from company records and measurements at the VDT workstations.

Mahram et al. (2013) studied multiple pregnancy outcomes; pregnancy duration and preterm birth, neonatal BW, length of newborn, head circumference and congenital malformations. The assessment of MF exposure was based on map information, MF measurements and questionnaires. No significant differences in the selected endpoints were observed between the two study groups, "exposed" and "unexposed" to ELF-EMF during pregnancy.

Proximity to power lines was used in the study of de Vocht et al. (2014) and de Vocht and Lee (2014) as a proxy for MF exposure. A distance of 50 m was used as the cut-off between exposed and unexposed subjects. These investigators examined whether close proximity to residential ELF-EMF sources would be associated with a reduction in BW and increased the risk of LBW, SGA and spontaneous preterm birth. Residential proximity to high voltage cables, overhead power lines, sub-stations or towers during pregnancy was calculated for 140,356 singleton live births with adjustment being made for maternal age, ethnicity, parity and for the part of the population, additionally for maternal smoking during pregnancy. A reduced average BW was found if the pregnant woman lived in close proximity to a source, and the reduction was largest for female births. No statistically significant increased risks for clinical birth outcomes were observed with residential proximity to the source. This study did not utilize any

alternative methods of exposure assessment other than distance to known ELF MF sources such as power lines or substations.

Residential proximity to power transmission lines was used to define MF exposure in the study of stillbirths conducted by Auger et al. (2012). OR for stillbirth at term was higher among those who lived near powerlines (<25 m) compared to the reference group ( $\geq$  100 m) (OR 2.25 (1.14-4.45)), but no apparent dose-response pattern was observed.

Overall, most of the epidemiological studies examining the association between MF exposure and adverse pregnancy outcomes have not evaluated in any systematic manner the validity of their exposure assessment and thus a misclassification of exposure may have influenced the conclusions emerging from these studies. Some recent studies have not applied any supplemental methods of exposure assessment other than distance to known ELF MF sources such as power lines or sub-stations. Although this does provide a crude estimate of average MF level, it is considered as poor predictor of actual MF exposure.

**Table 3. Studies on maternal exposure to extremely-low-frequency (ELF) MFs and pregnancy outcome.**

Study outcome	Study size (N; cases/controls)	MF exposure source	MF exposure assessment method	Result	Study
<b>Miscarriages</b>					
Miscarriage, case control	673 cases and 583 controls	Electric blankets and heated water beds	Telephone interview	Frequency of miscarriage correlated with presumed electric bed use	Wertheimer and Leeper (1986)
First-trimester miscarriage, case control	355 cases and 723 controls	Occupational VDT use	Interview	OR 1.8 (1.2-2.8) for > 20 h/wk	Goldhaber et al. (1988)
Miscarriage, cohort	2164; 4712 pregnancies	Occupational exposure to VDT	Exposure classified by job title.	OR 1.19 (1.09-130)	McDonald et al. (1988)
Miscarriage, cohort	1879 livebirths and 142 miscarriages	Ceiling cable heat, electrically heated beds	Questionnaire	Association with seasonal variation	Wertheimer and Leeper (1989)
First-trimester miscarriages, case control	439 cases, 909 controls	Occupational VDT use	Questionnaire on the occupational categories and use of VDT	OR 1.2 (0.88-1.6) for use of less than 20 hours per week and 1.2 (0.87-1.5) for 20 hours or more.	Windham et al. (1990)
Miscarriage, case control	191 cases and 394 controls	Occupational VDT use	MF measurements, questionnaire	OR 1.1 (0.7-1.6); OR (>0.9 $\mu$ T vs. <0.4 $\mu$ T) 3.4 (1.4-8.6).	Lindbohm et al. (1992)
EPL, nested case control	89 cases and 102 controls	Residential and occupational exposure	MF measurements at front door and in houses. Occupational MF measurements and job classification	RR 5.1 (1.0-25.0) for $\geq 0.63 \mu$ T RR 1.1 (0.6-1.9) for 0.1-0.62 $\mu$ T	Juutilainen et al. (1993)

Study outcome	Study size (N; cases/controls)	MF exposure source	MF assessment method	exposure	Result	Study
Miscarriage, case control	150 cases and 232 controls with measured MF; 245 cases and 248 controls with wire code	Residential exposure	MF measurements and wire codes	MF measurements and wire codes	OR 0.8 (0.3-2.7) for >0.2 $\mu$ T, Medium wire code: OR 0.6 (0.3-1.1) with medium wire code, and High wire code: OR 0.7 (0.3-1.8) with high wire code	Savitz and Ananth (1994)
Miscarriage, case control	508 cases and 1,148 controls	Occupational/Residential VDT	Questionnaire	Questionnaire	OR 1.0 (0.8-1.2)	Grasso et al. (1997)
Miscarriage, prospective study	2967	Residential exposure, heated water beds, electric blankets	Interviews and codes	Interviews and wire codes	Electric blankets RR 1.8(1.1-3.1); waterbeds RR 0.6 (0.4-1.1) or wire codes 0.4 (0.2-1.2) were not associated to increased risk.	Belanger et al. (1998)
Miscarriage; prospective study	5144	Electric blankets and waterbeds	MF measurements and questionnaire	MF measurements and questionnaire	Electric blankets: 0.8 (0.5-1.1) Waterbeds: 0.9 (0.7-1.2).	Lee et al. (2000)
Miscarriage; case control and prospective study	177 cases and 550 controls; 219 study subjects in a prospective sub-study	Residential exposure	Wire codes, area measures, and personal exposure measurements	Wire codes, area measures, and personal exposure measurements	Increased miscarriage risk with high ROC and maximum value, but also fields above 0.2 $\mu$ T OR 3.0 (1.1-8.4)	Lee et al. (2002)
Miscarriage, prospective study	969	Residential occupational exposure during 24-h	Personal and exposure diary	Personal LF MF measurements and diary	Maximum exposure > 1.6 $\mu$ T was associated to higher risk RR 1.8 (1.2-2.7); no association with 24-h TWA: RR 1.2 (0.7-2.2) with $\geq$ 0.3 $\mu$ T	Li et al., (2002)
Miscarriage, prospective	413	Residential exposure	Measurements at study subjects' front doors and in the alley in front of the subjects' houses	Measurements at study subjects' front doors and in the alley in front of the subjects' houses	RR 2.35 (1.18-4.71) with maximum alley exposure	Wang et al. (2013)

## Birth weight, small for gestational age, foetal growth

Study outcome	Study size (N; cases/controls)	MF exposure source	MF assessment method	exposure	Result	Study
Foetal growth, case control	4271	Electric blankets and heated waterbeds	Interview		Association with seasonal variation	Wertheimer and Leeper (1986)
LBW (<2500 g), IUGR, case control	405; cases: 13 (<20 h/wk) and 21 (≥20 h/wk)	Occupational VDT use	Occupational categories & reported use of VDT		LBW: OR 1.1 (0.52-2.1) <20 hr/wk and 1.4 (0.75-2.5) with ≥ 20h/wk IUGR: OR 1.6 (0.92-2.9)	Windham et al., (1990)
LBW (<2500 g), case control	150 cases and 232 controls with measured MF; 245 cases and 248 controls with wire code	Residential exposure	Interviews, MF measurements, wire code		LBW: OR 0.3 (0-2.4) with >0.2 μT LBW: OR 2.6 (1.2-6.5) with medium wire code; and 0.7 (0.2-2.3) with high wire code	Savitz and Ananth (1994)
LBW (<2500 g), IUGR, prospective study	2550	Occupational VDT use	Questionnaires and MF measurements		LBW: OR 1.4 (0.3-6.1) with ≥0.2 μT IUGR: OR 1.2 (0.4-3.1) with ≥0.2 μT	Bracken et al. (1995)
LBW (<2500 g), IUGR, prospective study	2967	Electrically heated beds (blankets & water beds)	Interview, MF measurements		LBW: no association; RR 0.9 (0.2-3.6) with ≥1.0 mG vs. < 1.0 mG and 1.4 (0.3-6.1) with ≥2.0 mG vs. <1.0 mG; IUGR: OR 1.6 (0.4-6.5) RR 0.6 (0.2-2.3) with ≥1.0 mG vs. < 1.0 mG and 1.2 (0.4-3.1) with ≥2.0 mG vs. <1.0 mG	Bracken et al. (1995)
LBW (≤2,800 g), cohort	284 telephone operators using	Occupational VDT exposure	VDT exposure evaluated from	was from	No association; for RBW OR 0.9 (0.5-1.7)	Grajewski et al., (1997)

Study outcome	Study size (N; cases/controls)	MF exposure source	MF assessment method	exposure	Result	Study
	VDTs, and 363 unexposed controls		company records and a sample of measurements. Also exposure times of 1-25 h/wk and >25 h/wk were assessed		OR 0.4 (0.1-1.0) with 1-25 h/wk OR 1.4(0.7-3.1) with $\geq$ 25 h/wk	
LBW, SGA, cohort	707215	Transmission lines	Proximity to power lines in distance categories		No association between residential proximity to transmission lines and LBW. A lower likelihood of SGA birth was present for some distance categories, for example, OR 0.88 (0.81 - 0.95) for 50 - 75 m relative to $\geq$ 400 m	Auger et al. (2010)
Foetal growth, cohort	222 exposed and 158 unexposed women	High voltage towers and cables	Map information was used to identify exposed and unexposed		No association	Mahram and Ghazavi (2013)
LBW, SGA, cohort	140356 live births	High voltage overhead power lines, substations or towers	Closest residential proximity to the sources during pregnancy was calculated		RBW, (significant) of 212 g (395-29 g) for close proximity to a source, and was largest for female births. After confounder adjustment (Vocht et al., 2014b) a reduction by 116 g (224-7 g).	de Vocht et al. (2014) and de Vocht and Lee (2014)

## Other effects

Study outcome	Study size (N; cases/controls)	MF exposure source	MF assessment method	exposure	Result	Study
Stillbirth, cohort	514826 live births and 2033 stillbirths	Residential exposure	Proximity to transmission lines.		OR 2.25 (1.14-4.45) with <25 m vs. $\geq 100$ m, no dose-response observed	Auger et al., (2012)
NTDs, cohort	23491	Electric blanket	Questionnaire		No effects, RR 1.2 (0.5-2.6)	Milunsky et al. (1992)
NTDs and oral cleft defects, case control	535 cases and 535 controls	Electric bed heaters	Questionnaire		OR 0.8 (0.3-2.1) for cleft palate, OR 0.7 (0.3-1.3) for cleft lip, and OR 0.9 (0.5-1.6) for neural tube defects	Dlugosz et al. (1992)
NTD, two case controls studies	538 NTD cases and 539 controls and 265 NTD cases and 481 controls, 652 orofacial cleft cases and 734 controls; 1455 cases, 1754 controls in total	Electric blankets, bed warmers, or heated waterbeds	Questionnaire		No association between exposure time to bed-heating devices and NTD or orofacial cleft; RR for electric blanket in study 1 1.8 (1.2-2.6) and in study 2 1.2 (0.6-2.3), water bed in Study 1 1.2 (0.8-1.8), and for water bed in study 2 1.2 (0.8-1.9)	Shaw et al. (1999)
CUTAs, case control	118 cases and 369 controls; women with history of subfertility	Residential VDT use, electric blankets, heated water beds	Interviews		OR 4.4 (0.9-22.7); first trimester exposure 10.0 (1.2-85.5)	Li et al. (1995)
CA, case control	11 cases and 22 controls	Power lines	Distance		OR 0.95 (0.45-2.03) with 100 m cut-off, and OR 1.25 (0.49-3.22) with 50 m cut-off	Robert et al. (1996)
SPTBs, cohort	140356	High voltage cables,	Closest residential		No increased risk with residential	de Vocht et al. (2014) and de

Study outcome	Study size (N; cases/controls)	MF exposure source	MF assessment method	exposure	Result	Study
PD (<37 weeks), case control	150 cases and 232 controls with measured MF; 245 cases and 248 controls with wire code	overhead power lines, substations or towers  Residential exposure	proximity to the sources during pregnancy was calculated  Interviews, measurements, wire configuration code	proximity of 50 m or less OR . 2.00 (0.61 – 6.59) for <50 m vs. < 400 m  OR 0.7 (0.1-4.0) with $\geq 0.2 \mu\text{T}$		Vocht and Lee (2014)  Savitz and Ananth (1994)
PTB (<37 weeks), cohort	284 telephone operators using VDTs, and 363 unexposed	Occupational VDT use	Company records and a sample of measurements, interviews		No association; PTB OR = 0.7(0.4-1.1)	Grajewski et al., (1997)
PTB and infant sex, cohort	707215	Transmission lines	Proximity to power lines in six distance categories		No association, for example OR for PTB 0.99 (0.92 - 1.07) with <50 m vs. $\geq 400$ m	Auger et al. (2010)
CA	Congenital abnormality	CUTA	Congenital urinary tract anomaly		SGA	Small-for-gestational age
EPL	Early pregnancy loss	IUGR	Intrauterine growth retardation		SPTB	Spontaneous preterm birth
LBW	Low birth weight	NTD	Neural tube defect		VDT	Video display terminal
OR	Odds ratio	PD, PTB	Preterm delivery/birth			
ROC	Rate of change	RR	Relative risk			



#### **1.4. AIMS OF THE PRESENT STUDY**

The aims of this study were to develop and evaluate methods for assessment of residential and occupational exposure to LF MFs, and to assess the possible association of ELF MF exposure with certain reproductive risks. The four original studies aimed at answering the following questions:

- I      What is the validity of short-term “spot” measurements in assessing longer term personal ELF MF exposure?
  
- II     Could short-term 20 min measurements be used for assessing temporal variability of residential ELF MF exposure?
  
- III    Is maternal residential ELF MF exposure associated with time to pregnancy, birth weight or small for gestational age?
  
- IV     How high are exposure levels to IF and ELF MFs in workers employed as cashiers, and could this occupational group serve as a basis for epidemiological studies addressing the possible health effects of IF MFs?

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## 6. *Discussion*

The aim of the present thesis was to study LF MFs in epidemiological studies, focusing on the validity of short-term measurements in the evaluation of residential and occupational exposures to ELF and IF MFs. In an epidemiological study, the association between maternal exposure to ELF MF and selected reproductive outcomes was studied. The results of the studies will be discussed below.



## **6.1. ASSESSMENT OF EXPOSURE TO RESIDENTIAL AND OCCUPATIONAL LOW FREQUENCY MAGNETIC FIELDS: VALIDITY OF SHORT-TERM MEASUREMENTS**

Short-term measurements of MFs are frequently used in epidemiological studies, although the validity of such measurements may be limited in estimating true personal exposure. The aim of Study I was to evaluate residential short-term spot measurements as surrogates for long term personal MF exposure. Spot measurements and 24-h personal MF measurements were conducted in 30 homes. The 24-h measurements were used as the gold standard, when evaluating the validity of various summary measures calculated from the spot measurements.

It was observed that the average of the spot measurements of a residence resulted in the smallest exposure measurement error (i.e. the smallest misclassification). In addition, the above bed spot value displayed a higher correlation with the 24-h exposure metrics than could be achieved with any room average. It was noted that spot measurements performed about equally well in predicting different types of 24-h exposure metrics (arithmetic mean, median, percentage of time above 0.15  $\mu\text{T}$ , and percentage of time above 0.29  $\mu\text{T}$ ).

In Study II, short-term measurements were conducted and tested with a new approach, where the person making spot measurements wore a recording MF meter during a 20-min visit to the residence. The goal was to evaluate the pros and cons of short-term measurements for estimating other exposure metrics. The validity of the selected exposure metrics calculated from the 20-min measurements was evaluated by comparing the values to the corresponding metrics calculated from the 24-h or 12h data. The measures of validity used were the Spearman correlation coefficient ( $r$ ), sensitivity, and specificity.

The Spearman correlation coefficients were, in general, lower than in studies where short-term measurements have been compared to long-term measurements conducted at a fixed point (Juutilainen et al., 1996; Schüz et al., 2000). The results also

indicated that exposure at home largely determined the 24-h exposure, which is also supported by the fact that the correlations between 12h and 24-h exposures were high for many of the exposure metrics. The 20-min measurement was modestly associated with standard deviation and rate of change metric, but provided very little information about other measurements evaluating temporal variations. The 20-min measurement was found to be useful also for assessing more conventional exposure metrics such as arithmetic mean and median, but it did not seem to offer any advantages compared to spot measurements in assessing this type of exposure metrics.

The results of Studies I and II show that spot measurements and the 20-minute measurements are correlated with 24-h exposure. However, short-term measurements can also lead to considerable misclassification of exposure. For example, about every third 20-min measurement misclassified the MF-exposure when compared to the 24-h measurement. This level of misclassification could introduce a considerable underestimation of the effect size, if there were a real association between MF exposure and the studied endpoints (Flegal et al. 1986, Armstrong 1995, Delpizzo and Borghesi 1995; White et al., 2008). However, the impact on effect size depends on the type of exposure measurement error (classical or Berkson error), as pointed out by Heid et al. (2004).

Because of the small sample size (number of acceptable 24-h measurements was 27), there is considerable uncertainty in the results of Studies I and II. For example, the Spearman correlation coefficient between average of spot measurements and 24-h mean was 0.77, but its 95 % confidence interval ranged from 0.55 to 0.89. This limitation was partly overcome by using several measures of validity and by using the entire pattern in the interpretation of results, but it is recommended that larger samples size should be incorporated into future studies.

In conclusion, the average of spot measurements in a residence performed best in estimating 24-h average personal MF exposure and time above threshold. It was found that a 20-min measurement provided some information about certain aspects of MF temporal variability (standard deviation and the

rate of change metric) and could be used for estimating other exposure metrics (arithmetic mean and median), but it was no better for this purpose than traditional spot measurements. Overall, the use of short-term measurements can lead to considerable misclassification of exposure, and epidemiologists using such measurements should be aware of the limitations of these approaches. Validity studies (such as conducted in Studies I and II of the present thesis) should be performed whenever possible to clarify the limitations of the exposure assessment methods.

## **6.2. EPIDEMIOLOGICAL STUDY ON MATERNAL EXPOSURE TO LOW FREQUENCY MAGNETIC FIELDS, TIME TO PREGNANCY AND BIRTH WEIGHT**

In Study III, possible associations were investigated between ELF MFs and time to pregnancy (TTP), low birth weight (LBW) and small for gestational age (SGA). TTP was included as delayed pregnancies might be at least partly related to early foetal loss, a phenomenon associated with ELF MF exposure in an earlier study (Juutilainen et al., 1993). This study was the first to address maternal exposure to residential and occupational ELF MF and TTP. The study cohort consisted of 526 mothers who gave birth between 1990 and 1994 in Kuopio University Hospital, Finland.

To increase the prevalence of high ELF MF exposure, women living in buildings near known ELF MF sources were included. Maternal exposure to ELF MF before and during pregnancy was assessed in two ways - with short-term measurements in their residences and with questionnaires. The associations between ELF MF exposure and TTP, LWB and SGA were analysed by logistic and linear regression, adjusting for factors known to be associated with the examined pregnancy outcomes, such as maternal smoking, alcohol consumption and socioeconomic status.

There were several strengths of the exposure assessment in Study III. The residential MF measurements were conducted by skilled persons who were blinded to the study subjects' pregnancy outcomes. Because of the validity studies (Studies I and II), the measurement error was known for the measurement-based exposure assessment. Information from the validity studies was also used in the selection of exposure metrics for the epidemiological study. The MF exposure was assessed both with measurements in residences and by questionnaires enquiring about exposure from appliances. However, the response rates to questionnaires were relatively low, and the quality of the questionnaire-based MF exposure assessment is not known. The questionnaire-based exposure

estimates may therefore be prone to misclassification and bias, and should be given less weight in interpreting the results.

Although the aim was to select the study group so that the prevalence of high exposures and exposure contrasts were increased, the MF exposures of the women were only slightly higher than in residences in general. This is a limitation of the study. Recall bias may have affected the exposure estimates obtained from the questionnaires sent after the pregnancy. The 6 month cut-off used for TTP is a potential source of misclassification of TTP. However, time to pregnancy was also analysed as a continuous dependent variable, and the results were consistent with the logistic regression analysis.

In conclusion, no association was detected between maternal ELF MF exposure and TTP, LBW or SGA. ELF MF exposure is not likely to be associated with TTP or prenatal growth at the residential exposure levels that were measured in this study. The ELF MF exposure of the mothers was slightly higher than in Finnish residences in general, but very high exposures ( $>0.4 \mu\text{T}$ ) were rare.

### **6.3. ASSESSMENT OF OCCUPATIONAL EXPOSURE TO MAGNETIC FIELDS FROM EAS DEVICES**

In Study IV, the goal was to study occupational exposure to LF MFs among cashiers. Intermediate frequency MFs were addressed because of the high numbers of electronic article surveillance (EAS) devices situated near to the cash-out tills in the stores. Exposure to ELF MF fields was assessed because cashiers work near many devices operating with 50 Hz electric power. A total of 31 cashiers were included in the study. In addition to the MF measurements, questionnaires were also used to obtain data.

Study IV applied two alternative ways to assess MF exposure and compliance with reference levels: broadband measurement of peak field (Jokela 2007) and the ICNIRP summation rule for multiple frequencies (ICNIRP, 2010). The results indicate that the ICNIRP summation rule may be unnecessarily conservative when

measuring complex waveforms such as EAS devices using a pulsed 58 kHz signal.

The measured peak magnetic flux density at the cashier's seat for IF MFs varied from 0.2 to 4  $\mu$ T, and ELF MFs from 0.03 to 4.5  $\mu$ T, which are much lower than recommended exposure limits (ICNIRP, 2010). Very short exposures to high IF MFs (maximum 189  $\mu$ T) occurred tens of times during each work-shift when the cashiers walked through the EAS gates. The highest values exceed the current occupational reference levels for IF (ICNIRP, 2010) and action levels by EU (EU, 2013). The minimum exposure time is not defined in these reference levels. Since the reference levels (set for external fields) are conservative and can be exceeded even when basic restrictions (for internal fields in the body) are not exceeded, further studies are recommended to determine compliance with basic restrictions.

This study combined measurements and questionnaires to assess cashiers' exposure to IF and ELF MFs and this approach was useful in the characterization of the importance of both behavioural patterns and field sources in cashiers' MF exposure: the workers may be exposed to high levels of IF MFs tens of times every day when walking through the EAS gates, and are almost continuously exposed to moderately elevated MF levels.

Employees working near EAS devices represent an exceptional group of workers with respect to exposure to MFs and this group could serve as a basis for future epidemiological studies investigating whether IF MFs exert any potential health effects, such as carcinogenicity, or adverse reproductive outcomes. One limitation of epidemiological studies has been the difficulty to identify a sufficiently large group of study subjects whose IF MF exposure is substantially higher than that of the general population. Clearly cashiers represent one such group of employees. An epidemiological study based on the measurements performed in this study is currently being undertaken within the GERoNiMO project funded by the FP7 of the European Union.

In conclusion, this study provided valuable information about cashiers' occupational exposure to low frequency MFs. It identified a group of workers that may serve as a basis of epidemiological



studies on the health effects of IF MFs, and provided exposure data that can be used for exposure assessment in epidemiological studies.

## 6.4. CONCLUSIONS

The following conclusions can be drawn from the present study

- I Spot measurements are useful in predicting the average magnetic field exposure and time above a threshold. The 20-min measurement did not confer any advantage compared to spot measurements, and it is not very useful for estimating magnetic field temporal variability or maximum exposure. Short-term measurements provide a useful method to assess exposure in epidemiological studies, but it is important to understand their limitations.
- II Performing validity studies is helpful for choosing the most appropriate exposure assessment method among the (typically approximate) methods that are feasible. Furthermore, quantification of exposure measurement error in the validity studies is helpful for the interpretation of epidemiological findings.
- III Of the short-term exposure assessment methods tested, average of the spot measurements in a residence was found to be the most appropriate for predicting personal exposure.
- IV The results did not support an association between maternal exposure to extremely low frequency magnetic fields and time to pregnancy or giving birth to babies who are small for gestational age.
- V Cashiers represent a large occupational group exposed to low frequency magnetic fields, and these workers can serve as an exposure group in epidemiological studies addressing the possible health effects of intermediate frequency magnetic fields.

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## TUOMO ESKELINEN

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*This thesis assessed residential and occupational extremely low frequency (ELF, frequencies below 300 Hz) and intermediate frequency (IF, 300 Hz-10 MHz) magnetic field exposures. Short-term measurements were shown to be useful methods in exposure assessment. Cashiers were found to be a group with exceptional IF magnetic field exposure. No association between ELF magnetic fields and reproductive outcomes was found in an epidemiological study.*



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**PUBLICATIONS OF  
THE UNIVERSITY OF EASTERN FINLAND**  
*Dissertations in Forestry and Natural Sciences*

ISBN 978-952-61-2139-0  
ISSN 1798-5668