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Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study

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Abstract

The rapid increase in mobile telephone use has generated concern about possible health risks related to radiofrequency electromagnetic fields from this technology. An interview-based case-control study with 2708 glioma and 2409 meningioma cases and matched controls was conducted in 13 countries using a common protocol.

A significantly decreased risk was seen in relation to ever having been a regular mobile phone user both for glioma (odds ratio (OR) 0.81, 95% confidence interval (CI): 0.70,0.94) and meningioma (OR 0.79; 95% CI: 0.68, 0.91), possibly reflecting participation bias or other methodological limitations. Odds ratios were below 1.0 for all deciles of lifetime number of phone calls and nine deciles of cumulative call time. While there was no evidence of dose-response, a significantly increased risk of glioma was seen among users in the highest decile of cumulative call time (OR 1.40; 95% CI: 1.03, 1.89). That risk was greatest among subjects with tumours in the temporal lobe, where RF absorption is generally highest, and among subjects who reported using their phones on the side of the head where their tumour occurred. Self-reports of phone use are, however, subject to considerable recall error. Sensitivity analyses conducted to evaluate the robustness of the findings generally showed similar results.

Overall, no increase in risk of either glioma or meningioma was observed in association with use of mobile phones. There were suggestions of an increased risk of glioma at the highest exposure levels, but biases and errors prevent a causal interpretation. The possible effects of long-term heavy use of mobile phones require further investigation.

UV-A radiation enhances melanoma metastasis in mice

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Extended abstract

Ultraviolet (UV) radiation is considered the major factor in skin cancer development (1). Due to the increasing popularity of skin tanning lamps, the potentially deleterious effects of solarium-derived UV radiation have become a public health concern, since the use of solaria has been linked to the development of melanoma, a particularly aggressive subtype of skin cancer (2,3). Melanoma is characterized by high risk of hematogenous metastases in the early stages of disease and it is the major reason for melanoma mortality. An understanding of the physiological consequences of UV exposure is of crucial importance in the prevention of melanoma. The possibility that UV radiation may affect melanoma metastasis has not been addressed widely, although it is known that some of the UV-induced cellular effects, such as the systemic immunosuppression (4,5), increased expression of matrix degrading enzymes (6) and adhesion molecules (7,8), are events that can mediate the autonomous growth of melanoma and possibly enhance the metastatic potential of the melanoma cells.

We have investigated the effect of solarium-derived UV-A (320-400 nm) irradiation on the metastatic capacity of mouse melanoma reporting possible link between UV radiation exposure and melanoma metastasis both *in vitro* (9) and *in vivo* (10). Previously we have shown that *in vitro* UV-A radiation enhances the metastatic properties of mouse melanoma B16 cell lines by increasing the adhesiveness of melanoma cells to endothelium and changing expression of adhesion molecules. We have also shown that *in vivo* UV-A exposure of mice increases the formation of melanoma lung metastases in C57BL/6 mice injected *i.v.* with low-metastatic B16-F1 cells. Obtained results have confirmed that mice, that were *i.v.* injected with B16-F1 cells and exposed to UV-A, developed 14 days after treatment 4-times more of lung metastases as compared with the non-exposed group. However, the *in vitro* exposure of melanoma cells, prior to injection into mice, lead to induction only of 1.5-times more metastases as compared with the animals injected with non-irradiated cells. Therefore, UV-A-induced changes in the adhesive properties of melanoma cells cannot, alone, account for metastasis increase observed after *in vivo* exposure of mice.

The fate of the melanoma cells in mice circulation and the body during the first hours as well as days after melanoma cell injection remains obscure in the used mouse model. Although *in vitro* systems to assess melanoma metastasis exist, these systems do not adequately reflect the complexity of the in vivo microenvironment. Similarly, the rapid changes in cell surface molecule expression that occur in dynamic systems are most effectively observed in real time *in vivo*. Therefore the next step was to investigate the metastatic process in real time and to determine how an *in vivo* UV exposure of the mouse affects the melanoma cell circulation kinetics, cell trafficking to the host-organs, and their long-term ability to form metastases utilizing different *in vivo* molecular imaging technologies.

In vivo flow cytometer (IVFC) is an excellent tool with the capability to count circulating fluorescently labeled cells in living animals (11,12), since the migration of cell population of the interest can be observed in the native environment without the need to draw blood samples. Since the circulation kinetics of the B16 melanoma cells in this experimental metastasis model was totally unknown, the depletion rate of the fluorescent-labeled cells was determined using the IVFC technique. Melanoma cells were cleared very fast from mouse circulation and mainly for this reason no significant changes in the cell clearance were found between the UV-exposed mice as compared to the non-exposed controls.

To assess the localization of the B16 melanoma cells after the UV irradiation, the short term trafficking into the lungs during the first hours after melanoma cell injection was studied by non-invasive *in vivo* biochemiluminiscense system that allows the whole body imaging. Bioluminescence imaging showed increased melanoma cell arrest in the lungs 60 minutes after UV-A exposure compared to controls. As a long-term effect of the UV exposure on melanoma cells, UV-A irradiation was also shown to enhance remarkably the proliferation of B16-F1 cells in the lung parenchyma as compared to the non-exposed group during the next 15 days.

As conclusion we suggest that UV-A-derived increase of metastasis *in vivo* might be a combination of enhanced adhesion to pulmonary vasculature and enhanced proliferation that both contribute to the observed UV-A effect on melanoma metastasis. These results presented in this study suggest that, if occurring also in humans, exposure to UVA radiation during extensive sunbathing or solaria tanning periods might have the potential to cause increase in the hematogenous melanoma metastasis in patients with metastatic disease, but this needs to be confirmed in the future studies.

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Investigation of sun habits in Sweden 2005–2009

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Abstract
Between the years 2005-2009 a questionnaire has been used by the Swedish Radiation Safety Authority in order to see how much UV-radiation the Swedish population is exposed to. This Questionnaire has also made it possible to learn about how the sun habits for the Swedish population, their attitudes and knowledge about UV-related matter. A description of the method used will be presented together with result and discussion about what can be said about the years the questionnaire has been used. The questionnaire has been distributed to 2000 persons in Sweden and is collected by the Statistics Sweden, which also summarizes the results.

Introduction
Sweden has an environmental goal which states that the annual skin cancer incidence shall not be higher in the year 2020 than it was in 2000. A reason for setting up this goal is the fact that skin cancer is one of the fastest increasing types of cancer in Sweden and the main cause for this is the exposure of UV-radiation.

This goal is followed by two indicators, the annual number of skin cancer incidence and the exposure of UV-radiation of the population. The disadvantage of the annual skin cancer incidence as an indicator is that it does not correlate with the exposure of UV-radiation today. The delay between the damage and the onset of skin cancer makes it hard to draw any conclusions from the exposure today and the skin cancer incidence. In order see the actual exposure of UV-radiation one cannot rely on the incoming radiation alone but the crucial part is the behaviour and attitude when it comes to the sun or solarium.

This paper will present the model and questionnaire being used in order to estimate the actual exposure of the Swedish population as well as get knowledge about sun habits.

The indicator for the environmental work reflects how much UV radiation people are exposed to, depending on their behaviour. There are two interesting aspects of exposure to consider, first, the total exposure for the population (population exposure) and the extent of the exposure (burns). Both of these aspects are linked to the risk of getting skin cancer.

The questionnaire also provides information on attitudes toward sun exposure and various protective behaviours, knowledge about ultraviolet radiation and skin cancer. The work with the questionnaire began in autumn 2004 with the participant Katarina

Yuen, Lars-Erik Paulsson and Ulf Wester from SSI[1] and Richard Bränström from Karolinska Institutet (KI) and Helena Bäckström from Statistics Sweden (SCB).

Material and methods

When the purpose of the questionnaire was established the variables that would be used was determined. This section presents the approach when the exposure model and questionnaire was designed. As a first step a decision was made to construct at model that was rough but more easy to work with instead of a model with high precision which would increase the cost and workload. Because of the roughness in the model it is best to compare the results only from the same questionnaire, even though the exposure can be expressed in physical units. The exposure can be based on the following factors:

The duration of our time outside when the sun is reasonably strong.
What we use to protect ourselves from the radiation.
Exposure from other sources than the sun. (Solarium).

The model

The model takes into account behavioural aspects of the exposure and not weather conditions. It is based on MED, minimal erythemal dose where MED is the dose of UV-radiation that barely gives a redness on the skin and should in principle be decided for every individual and situation. Here MED is set as 210 J_{CIE}/m^2 (weighted erythemal dose). The coefficients used in the model has been chosen in order to give the exposure a physical quantity. The simplifications and assumptions in the model make it difficult to speak about the calculated exposure in terms of MED. Therefore the exposure is simply named the exposure in this paper. The exposure can vary between 0 and 1372,5.

Sunprotection

The protection from the sun can be divided into three components, surface, intensity and frequency. Surface means how large part of the skin that are being protected. For example some clothes only cover parts of the body, and the parts that are unprotected is exposed to the radiation that the current environment. The parts that are covered can still be exposed to the radiation depending on the fabric. Intensity takes into account the intensity of the sun and how much the UV-radiation is filtered by the protection. This concerns sparse, thin fabrics and its sun protective properties, badly applicated sunscreen etc. Frequency is how often a protection is being used.

The questions in the questionnaire is for a general situation with beautiful summer weather, i.e. no division for different situations as working time, free time or time abroad. The model assumes mainly free time. But different weights are used for free time and work time since it is reasonable to assume more clothes and shadow in a working environment. Since the model lacks precision, an estimate for the protective properties for different sun protective means as the size of hats, densities of the clothes etc. is built upon reasoning rather than measurement. For example shorts and t-shirts

[1] In July 2008 the Swedish Nuclear Power Inspectorate (SKI) and the Swedish Radiation Protection Institute (SSI) merged into the Swedish Radiation Safety Authority (SSM)

give a protection up to 50 %, scattered radiation can still reach people in the shadow and a protection of about 50 % can be assumed.

One question is concerning how many hours one usually spends outside a day with beautiful weather. The question is limited between 10 am and 4 pm between May and August. A division is made between a working day and a free day/weekend in Sweden and a free day abroad. Weeks of vacation in Sweden and abroad can also be extracted.

Even though the current weather conditions was not included in the model maps from the SMHI (Swedish Meteorological and Hydrological Institute) were studied for the years 1961 – 1990 in order to get a reasonable estimation for weather reduction. From these maps the weather reduction was set as 0,5.

The Exposure outside

The average UV-index in Sweden for the period of interest was approximately 3. One UV-index represents 90 J/(m^2h) erythemal UV-radiation against a horizontal surface i.e. 0,4 MED/h. Thus UV-index 3 corresponds to 1,3 MED/h. But for a realistic situation a person does not expose the entire body to UV-radiation at the same time. The fact that radiation before 10 am and after 4 pm can be of importance 1 MED/h was chosen for the exposure in Sweden and 2 MED/h for the exposure abroad.

Today, most of the sun bed used are full body tanning devices and most people tan with very little clothes. In this case it is reasonable to consider the entire body exposed to the radiation. In the model 2,5 MED/h was used for one tanning session in a solarium.

Results

The exposure

The exposure has been calculated according to the above mentioned model and is shown in figure1 and 2 for the years 2005-2009. During these years the exposure is relatively constant and no tendencies can be seen. The contribution from trips abroad to the exposure is relatively high. If you compare the different age groups from 2009 it is clear that the group with ages 18-24 has the highest degree of exposure. Generally the exposure is decreasing with increasing age.

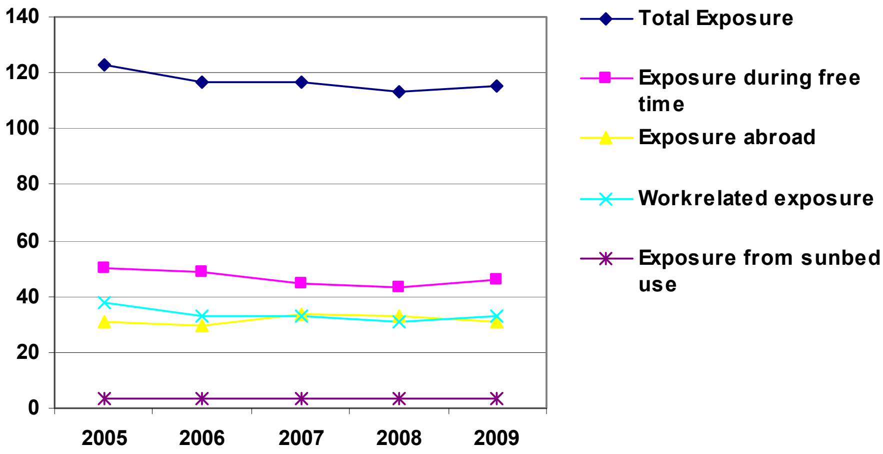

Fig. 1. UV-exposure for the years 2005-2009.

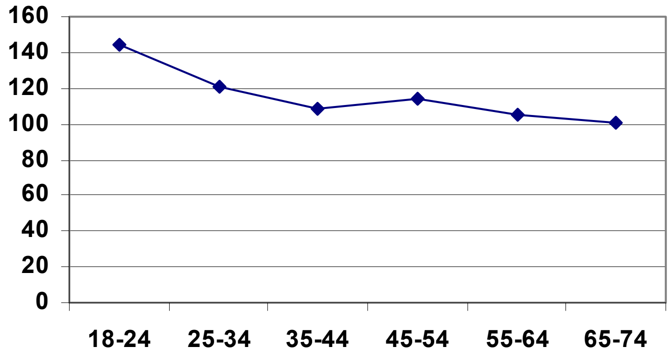

Fig. 2. UV-exposure for the year 2009 divided into different age groups.

Burns

Apart from the total exposure of UV-radiation the burns from UV-exposure is a riskfactor for skincancer. The most common places for getting a sunburn were a garden or balcony and a beach in sweden. Being burned abroad and on a lake was almost just as common.

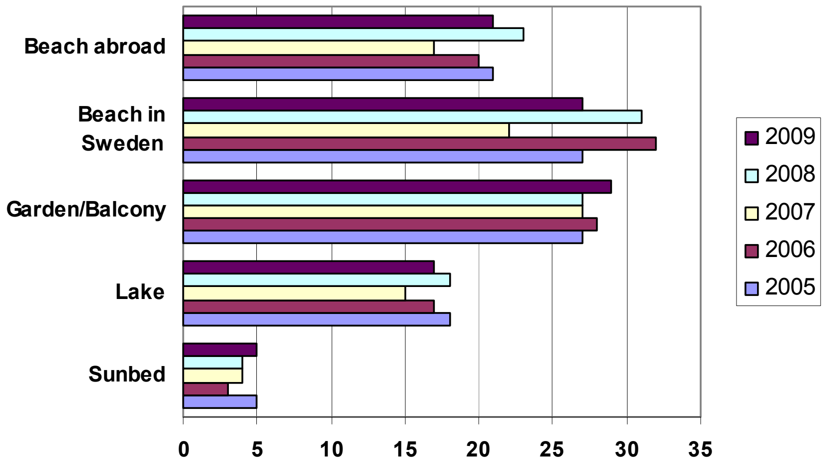

Fig. 3. Percentage of people suffering from sunburn at different locations for the years 2005-2009.

Protection

There are several ways to protect oneself from the sun. For example you could stay in the shade, avoid being outside in the middle of the day, using sunglasses, wearing clothes, cap or a hat or use sunscreen. As is shown below the most common protective behaviour is to wear clothes and the least common behaviour is to avoid being outside in the middle of the day.

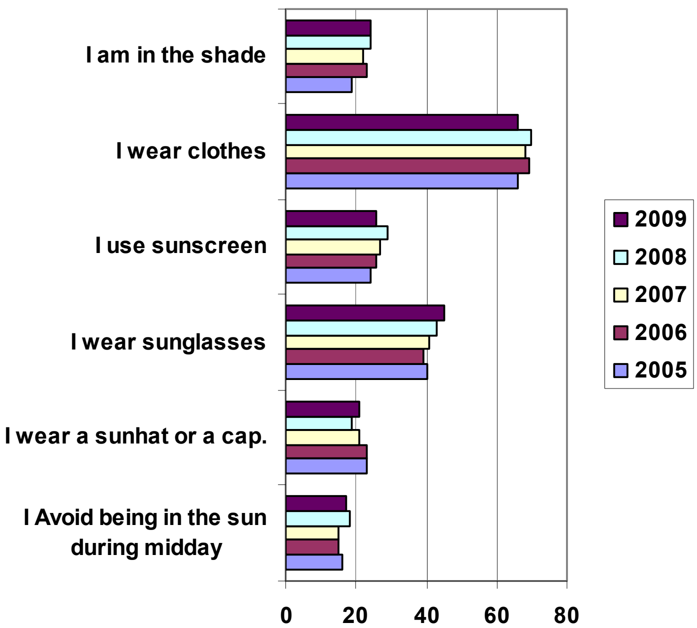

Fig. 4. Percentage of the respondents that always or often protect oneself in different ways.

Attitudes

The most important factor for how much UV-radiation the population is exposed to comes from the behaviour in the sun. There has not been any drastic change between the years 2005 and 2009. Most people enjoy being in the sun and try not to burn themselves. About two thirds think they look better and feel healthier when they have a tan and these statements are truer for women than men. One third worries about getting skin cancer. For the different age groups one can see that the youngest age group compare to the older ones think that using clothes as sun protection is more uncomfortable but the oldest age groups think using a sunscreen is more uncomfortable than the youngest age group.

Knowledge

The knowledge about the sun, skin cancer and other related topics is relatively high. Almost everyone knows that the sun can cause skin cancer and that children are more sensitive to the rays of the sun. There are no drastic differences between the age groups but one might see tendencies that women has a little more knowledge about matters that concerns health.

Discussion

A summary of the questionnaire and its results gives a relatively good overview of the sun habits in Sweden. But so far it is hard to see any obvious trends. Because of this, the questionnaire will not be sent out annually but every second or third year. Not unexpectedly the group with the greatest risk behaviour is the people in the youngest age group. The reasons why people act in a way they know can be harmful most likely depend on several factors. In terms of acute injuries there is only sunburn and possibly some eye damage, but these usually heal reasonable quick and therefore it is probably not a great concern for most people. The long time effect of UV-exposure and burns, skin cancer and cataract, usually lies way ahead in the future and does not affect the behaviour when you go to the beach or work in the garden.

Apart from the indicator for the UV-exposure and knowledge about sun habits and attitudes the data from the questionnaire has been used in press releases every year it has been sent out. For example:

2005: “Every second person burn during sun vacation!”
2006: “Every fourth Swede burn in sun when gardening!”
2007: “Risks well known, but sun sense practice rare (1 of 3)!”
2008: “Small improvement of sun habits! Sunburns down 6%”
2009: “Sun bed burns doubled among young persons!”

Conclusions

The Questionnaire will not be sent out annually but every second or third year. This gives the opportunity to make more specific studies that can focus on the potential risk groups. Since the risk behaviour is the “worst” in the youngest age group generally it would be interesting to see how the behaviour is for even younger ages. In order for the authority to give proper advice and information it is necessary to continue this kind of study.

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Role of modulation in the biological effects of radiofrequency radiation

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Abstract

The biological effects of modulated radiofrequency (RF) radiation have been a subject of debate since early publications more than thirty years ago, suggesting that relatively weak amplitude-modulated (AM) RF electromagnetic fields have specific biological effects different from the well-known thermal effects of strong radiofrequency energy. This discussion has been recently activated by the increasing human exposure to RF radiation from wireless communication systems. Modulation is used in all wireless communication systems to enable the signal to carry information. A previous review in 1998 indicated that experimental evidence for modulation-specific effects of RF energy is weak. This paper reviews recent studies (published after 1998) on the biological effects of modulated RF radiation. The focus is on studies that have compared the effects of modulated and unmodulated (continuous-wave, CW) RF fields; studies that have used only modulated or only CW signals are not included. While the majority of recent studies have reported no modulation-specific effects, there are a few interesting exceptions that warrant follow-up studies.

Location of glioma in relation to mobile phone use

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Abstract

The objective of our study was to evaluate whether the gliomas within the brain differ between mobile phone users and never-users. The energy absorbed from the radiofrequency (RF) electromagnetic fields of mobile phones depends strongly on the distance from the source. We would expect gliomas among users to be located nearer to the source of exposure i.e. mobile phones if such exposure increases the risk of gliomas. We used case-case analysis to evaluate whether location of the gliomas in the brain is related to the source of RF exposure. The study methods applied were novel and provide an improved approach to studying focal effects in the etiology of gliomas. By utilizing information on the tumor location instead of only amount of mobile phone use as in earlier studies, the case-case method enables focusing on SAR distribution of RF field. This offers a possibility to study biologically and physically more meaningful and refined hypotheses. The data consisted of 888 gliomas from seven countries with tumor mid-points assigned by neuroradiologists on a three-dimensional (1 x 1 x 1 cm) grid based on radiological images. The typical position of the mobile phone while used was assumed to be in the line from the external acoustic meatus to the corner of the mouth and distance was computed between this line and the mid-point of the tumor. The data analyses were made using unconditional logistic regression with distance as a categorical outcome (5 cm as a cut-point) in the case-case approach. In the case-case analyses never-regular users and those using mobile phone at the opposite side as the tumor had their gliomas nearest to the exposure line, but the differences were statistically non-significant. Our results do not suggest gliomas being located in excess in those parts of the brain with the highest exposure to the RF field of mobile phones.

Background

Mobile phones emit radiofrequency (RF) electromagnetic fields. RF fields have not been shown to be tumorigenic, but their biological and health effects have not been firmly established so far (Ahlbom et al. 2009). The energy absorbed from the RF fields of mobile phones depends strongly on distance from the source decreasing to one tenth in 5 cm of tissue (Cardis et al. 2008).

As the RF field emitted by the mobile phones penetrates the brain in a highly localized fashion, a local effect restricted to the part of the brain closest to the handset would be expected, if there is one. Instead of concentrating on crude indicators of phone use (such as self-reported number and duration of calls) as in most previous studies, utilizing the accurate tumor location enables focusing on the postulated distribution of the RF field within the brain, thus offering a biologically and physically more meaningful and more specific approach. However, only a few studies have assessed the location of glioma in relation to mobile phone use (Takebayashi et al. 2008, Hartikka et al. 2009), and these studies are based on small sample sizes.

The objective of the study was to evaluate whether gliomas among phone users occur preferentially in the areas of the brain having the highest RF exposure from the handset.

Methods

This study is based on data from seven European centers (nationwide studies in Denmark, Finland, Norway, Sweden; Bielefeld, Heidelberg and Mainz regions in Germany; Rome, Italy; and Thames region of Southeast England) within the Interphone study, an international collaborative case-control study, whose main objective was to assess whether mobile phones increase the risk of brain tumors (Cardis et al. 2007).

The study included 888 gliomas (61% of all glioma cases diagnosed during the study-period) diagnosed between September 2000 and January 2004 with tumor mid-point(s) assigned on a three-dimensional grid (1 x 1 x 1 cm). These mid-point(s) were defined by neuroradiologists, blind to the data on mobile phone, based on radiologic images.

The main exposure indicator in the analyses was the shortest estimated distance from the mid-point of the glioma to the putative source of exposure, i.e. typical location of the phone. The exposure line was assigned as a line from the external orifice of the ear canal to the corner of the mouth with the entire phone regarded as the source of exposure (as most phones have an integrated antenna with the whole body of the phone emitting an RF field). To avoid potential recall bias, distance was calculated to the nearest source of exposure on the same side as the glioma was located, irrespective of the patient's reported typical side of use.

Case-case analyses were carried out using unconditional logistic regression with distance between the mid-point of the glioma and the putative source of exposure (location of the phone) as a binary outcome (≤5 cm, >5 cm). Exposure indicators analyzed included regular use of mobile phone (regular use defined as ≥1 call/week for ≥6 months, use in the 6 months prior to glioma diagnosis excluded), cumulative call-time (divided into tertiles: 0.001-46 hours, 46-339 h and >339 h, with median of 133 hours and maximum of 20,000 hours), laterality (preferred side of use) and duration of use (cut-points chosen to correspond to those in previous studies: 6 months to 5 years, 5 to 9 years and 10 or more years of use). Never-regular use of a mobile phone was the unexposed reference category in all analyses. All analyses were adjusted for country, sex, age group and socioeconomic status.

Results

Information on mobile phone use was obtained from 98% of the cases, with 57% regular mobile phone users and 43% reporting no regular use. Laterality of use was known for 490 cases (99% of all regular users).

The mean distance between the tumor mid-point and the phone (for all gliomas, 6.25 cm) did not vary substantially by the indicators of mobile phone use. The mean distance was somewhat shorter among cases who had not used a phone regularly (6.19 cm) and those reporting the preferred side of use as contralateral to the tumor (6.29 cm) in comparison to regular (6.29 cm) and ipsilateral (6.37 cm) use. The mean distance was slightly longer for those with the highest cumulative call-time or those having used mobile phone for more than ten years, but the differences were not significant.

In the case-case analysis, using unconditional logistic regression with categorical distance as the outcome (≤5 cm, >5 cm), non-significantly decreased ORs for gliomas located within 5 cm of the presumed phone location were found in regular users compared with never-regular users (OR 0.87 (95% CI 0.63-1.20)). The odds ratios for higher exposure were below unity for all exposure variables in these analyses, indicating no excess in the highly exposed parts among regular vs. never-regular users.

Conclusion

Our results do not support the hypothesis of gliomas among users of mobile phones being preferentially located in the parts of the brain with the highest RF exposure from mobile phones. In the case-case analyses, gliomas among never-regular users, representing lower RF exposures, had a shorter mean distance between tumor mid-point and the presumed source of exposure than regular users. Consistent findings indicating no increased frequency of gliomas in the areas closest to the typical position of the mobile phone handset were observed with all exposure characteristics, e.g. cumulative call-time and duration of use.

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Hyperthermia-induced proliferative response in human cancer cell lines is counteracted by a 2.2 GHz pulsed signal

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Abstract
The present study describes the cell growth response of two human cancer cell lines, HepG2 and NB69, to 24-h simultaneous exposure to two physical agents: mild hyperthermia and 2.2-GHz, pulse-modulated, radar-like radiofrequency (RF) signals. The samples were sham-exposed or RF-exposed simultaneously inside two identical waveguides placed in a CO_2 incubator set at 37 ºC (standard temperature) or 38 ºC (mild hyperthermia). A complete discretized model of the setup was created for numerical dosimetry using FDTD software SEMCAD X. The average dose of RF radiation absorbed by the cultures was calculated to be subthermal ($\Delta T < 0.1$ ºC). At the end of the 24 h treatment the cell growth was analyzed through Trypan blue exclusion and cytometry. At 37 ºC the NB69 line responded to the RF exposure with a consistent reduction in cell number (13.5% % below controls; $p<0.001$) together with slight but significant changes in the kinetics of the cell cycle. In contrast, the HepG2 cell growth and cell cycle were not changed after the RF treatment. The + 1 ºC thermal stimulus alone induced significant increases in the number of cells in both NB69 and HepG2 lines (17.9% $p< 0.05$ and 18.8%, $p < 0.01$ above controls at 37 ºC, respectively). This cytoproliferative, thermally-induced response was blocked in both cell lines by the simultaneous exposure to RF. Consequently, the results indicate that under standard temperature conditions the HepG2 line is not responsive to the cytostatic effect exerted by the RF exposure in NB69 cells, whereas, under thermal stimulation of cell proliferation, both lines showed a similar, cytostatic response to RF, likely to be mediated by changes in the cell cycle. Studies are in progress investigating the mechanistic and molecular basis of the herein described cellular response.

Introduction
The study of the potential hazards of chronic exposure to weak, radiofrequency (RF) electromagnetic fields in residential or occupational environments has been addressed by a number of epidemiological studies (see Hietanen, 2006; Hardell and Sage, 2008 for recent reviews) and experimental investigations (Garaj-Vrhovac and Orescanin,

2009; Xu et al., 2010). RF fields in the GHz range are of particular interest because of the rapid implantation of recent and emerging telecommunication technologies. International regulatory bodies like ICNIRP or the European Council (ICNIRP, 1998; EU Council Recommendation, 1999) have developed their standards for protection of the public and workers against non ionizing radiation on the basis that only RF doses inducing thermal increases $\Delta T \geq 1$ ^{o}C in the exposed tissues can be considered detrimental to humans. There is general agreement that the energy at which most RF telecommunication signals are emitted are too low to induce significant thermal increases in the tissues of potentially exposed individuals (Hietanen, 2006). Consequently, it has been widely assumed that under normal conditions in residential and occupational environments, the exposure to RF radiation at subthermal doses can be considered safe. This assumption is supported by data from a large body of experimental studies that have failed to detect potential harmful effects of weak RF signals on a number of in vitro biological models (Higashicubo et al., 2001; Chauhan et al., 2007; Prisco et al., 2008).

On the other hand, several experimental studies have reported effects on cell cycle control and apoptosis (Marinelli et al., 2004; Joubert et al., 2008), on gene expression (Remondini et al., 2006; Buttiglione et al., 2007), and tumorigenesis (Repacholi et al., 1997) in different biosystems exposed to RF at doses estimated to be subthermal. This data would provide limited support to some epidemiological results indicating that chronic exposure to weak RF fields could represent a risk factor in the etiology of a number of ailments, ranging from perceived electromagnetic hypersensitivity or neurological symptoms to neurodegenerative diseases or different cancer types (Rubin et al., 2006; Sage and Carpenter, 2009). Taken together, both blocks of epidemiological and experimental evidence seem to be indicative that different, presently undetermined factors may be responsible for the controversial data obtained so far. Even if subthermal mechanisms of RF interaction existed, at high power densities the thermal effects would prevail, leading to adverse consequences. At lower exposure levels biological effects have been reported but, due to limitations in modeling and dosimetry, the possibility cannot be ruled out that thermal mechanisms could also intervene in the biological response. Under the present circumstances there is general consensus that experimental studies using sensitive biological models are crucial to the study of the thermal/subthermal mechanisms underlying the bioeffects of weak RF fields. The present study investigates the cell growth response of two human cancer cell lines, HepG2 from hepatocarcinoma and NB69 from neuroblastoma, that have been reported to be sensitive to RF fields (Hernández-Bule et al., 2007; Trillo et al., 2009). The cells were exposed for 24 hours to a 2.2 GHz, pulse-modulated radar-like signal with high instantaneous amplitude and very low average power. Little is known on the biological interactions of this type of signals, and their potential relevance to the human health needs to be more efficiently addressed by the standards for radiation protection. Additionally, in order to determine whether a potential response to the RF exposure could be mediated by thermal phenomena, a set of experiments was conducted in which cell cultures were exposed to the RF treatment and/or incubated under mild hyperthermia (38 ^{o}C).

Material and methods

Exposure System

The schematic view of the RF exposure equipment is shown in Figure 1. The system has been described in a previous paper by Varela et al. (2010). Briefly, the system consists of: 1) A signal generator (MCL 15156, MCL Inc, USA) in the 2.0 – 2.5 GHz band, with specification for CW power ≥ 35 W and pulse duration ≥ 5 µs; 2) A modulator that controls the pulse duration and repetition rate; 3) A double rectangular waveguide applicator (95 x 45 mm section, 500 mm in length) connected to a high power matched load; 4) Ancillary equipment composed of a RF counter HP-5347A, a power meter HP-432A and a detector for pulse shape control.

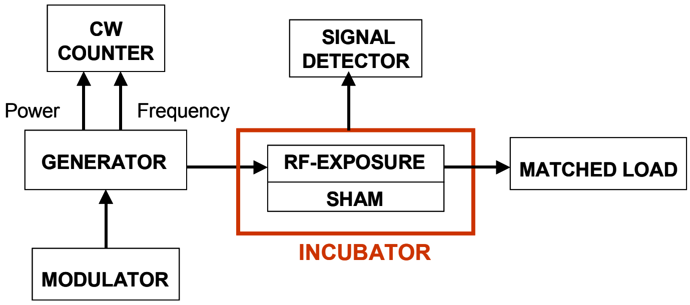

Figure 1.- Diagram describing the configuration of the System: The electromagnetic signal is generated by a signal generator sweep oscillator ranging 1 - 3 GHz. The RF applicator is located inside a CO_2 incubator and is composed of two waveguides, one for RF-exposure and another for sham-exposed control samples.

The RF applicator

During RF- or sham-exposure the samples are placed on a double-shelf Teflon support holding eight Petri dishes, inside each of the two wave guides (Fig. 2). Both guides have a lateral, copper hinged section and are closed by slotted short circuits equipped with fans, for temperature homogeneity and proper atmosphere exchange within the guides. A coaxial probe in the centre of the top wall waveguide is used for monitoring the parameters of the RF signal applied to the cells. Since all in vitro procedures have to be conducted in sterile conditions, the waveguides, sensors, connectors, holders and wiring were designed and built to withstand the 9-hour incubator routine for inner decontamination at 90 °C and RH > 95%.

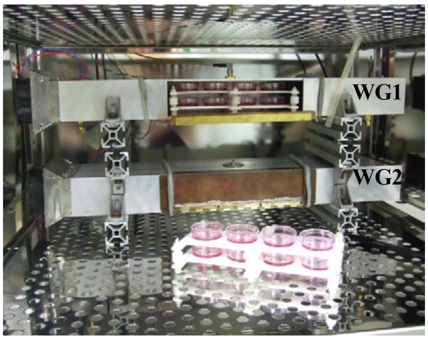

Figure 2. Waveguide pair for simultaneous RF- and sham-exposure within a CO_2 incubator. The trapdoor to the upper waveguide (WG1) has been opened to show the holder with Petri dishes. The 8-dish holder corresponding to WG2 is displayed outside the guide.

RF signal and dosimetry

The dosimetric procedures and results have been described in detail by Varela et al. (2010). Briefly, a 28 W (CW), 2.2-GHz, pulse-modulated (5 µs pulse duration, 100 Hz repetition rate) signal was applied to cell cultures grown in 35-mm Ø plastic Petri dishes, where the cells formed a monolayer on the bottom of the dishes. Dosimetric calculations were performed after a homogeneous model of the exposed materials, considering the dishes filled with 1.5 ml of lossy medium with relative dielectric constant $\varepsilon r = 77.5$ and electric conductivity $\sigma = 2.3$ S/m, and taking into account the presence of a meniscus at the surface of the culture medium. The Finite-Difference Time-Domain (FDTD) method was used to calculate the SAR distribution in the cell cultures through commercial software SEMCAD X (Schmidt & Partner Eng. AG, Zurich, Switzerland). The space-averaged SAR for CW exposure was calculated to be 46 W/kg. Since the samples were exposed to 5-µs pulses at a 100 pps repetition rate, the estimated time-averaged SAR would be 23 mW/kg. Considering that the experiments were conducted under strict temperature control and taking into account the damping thermal effect of the heat diffusion, we can assume that in our experiments the RF stimulus was applied at a dose well below those at which significant thermal effects can be expected.

Cell Culture

The human hepatocarcinoma cell line HepG2 obtained from the European Collection of Cell Cultures (ECACC, Salisbury, UK) was grown in Dulbecco's modified Eagle's medium (D-MEM, BioWhittaker-Lonza, Verviers, Belgium) supplemented with 10% heat-inactivated Foetal Calf Serum (FCS, GIBCO-Invitrogen, Paisley, Scotland, UK), 2 mM L-glutamine, and 100 U/ml penicillin - streptomycin. The human neuroblastoma cell line NB69, obtained from ECACC, was cultured in D-MEM medium supplemented with 15% heat-inactivated FCS, 4 mM L-Glutamine, 100 U/ml penicillin – streptomycin and 0.25 µg/ml amphotericin B. The media were always pre-heated at 37 ºC in order to avoid abrupt temperature changes that could induce cellular stress. In all experimental runs, four days prior to RF exposure, HepG2 or NB69 cells were aliquoted from a single parental flask to individual 35-mm Ø Petri dishes at densities of 9×10^4 or 7×10^4 cells per millilitre of medium, respectively, and grown in a humidified atmosphere with 5% CO_2 at 37 ºC.

Cell Growth and cell Viability Analyses

HepG2 or NB69 cells at a 60% confluence (day 4 after plating), were transferred in sterile conditions to the experimental incubators and grown inside/outside energized/unenergized waveguides. In all experimental runs, two cell culture samples were incubated simultaneously: A group of 8 Petri dishes was grown inside WG1 (Fig. 2) and an identical, 8-dish group was incubated inside WG2. In a set of experiments investigating the cellular response to mild hyperthermia, a third group of 8 control dishes was grown simultaneously inside an identical, separate CO_2 incubator, at a 37 ºC temperature. At the end of the 24-hour incubation the cells were detached from the dishes, resuspended in 1 ml of medium and studied for viability and proliferation. The number of alive and dead cells was determined through haemocytometer analysis of 50-

µl aliquots. Each sample was double-counted using the Trypan blue exclusion method. All experimental procedures and analyses were conducted in the blind.

Flow cytometry (FACS)

Cell samples grown for 24 hours with or without RF stimulation were harvested and fixed in 70% ethyl alcohol at room temperature for 4 hours. Subsequently, the cells were treated with RNAse-DNAse free (100 µg/µl; Roche) and stained with the fluorescent dye propidium iodide (IP, 20 µg/ml; Boehringer-Manheim) for 1 hour at room temperature. The relative fractions of cellular subpopulations in different phases of the cell cycle were determined through quantification of DNA content by flow cytometry, using Becton-Dickinson FACScan (FACScalibur, Becton Dickinson, Franklin Lakes, NJ, USA). Cell cycle parameters were determined by CellQuest 3.2 Software (Becton Dickinson Immunocytometry Systems, San Jose, CA, USA). Twenty thousand cells per sample were analyzed.

Statistical Analysis

Data was expressed as mean ± standard error (SEM) of at least three independent replicates, using GraphPad Prism software (GraphPad Software, Inc., San Diego, CA). The ANOVA test followed by two tailed Student's t-test was applied. Statistical significance was set at $p < 0.05$.

Results

Viability and cell growth response to the RF signal at standard temperature

Fig. 3 summarizes the cell growth response of the HepG2 and NB69 cell lines to the RF treatment at standard conditions of temperature (37 ºC). In the HepG2 line, at the end of the 24-h RF treatment no significant differences were observed with respect to sham-exposed controls. In contrast, NB69 cells responded to the same RF treatment with a consistent, statistically significant reduction (13.5% below sham, $p<0.001$) in the total number of cells (Fig. 3). This effect was accompanied with a modest, thought statistically significant increase in the proportion of necrotic cells in the exposed samples (15.9 ± 2.1%; $p<0.01$) when compared to the respective sham-exposed samples (spontaneous death rate: 13.9 ± 2.0%).

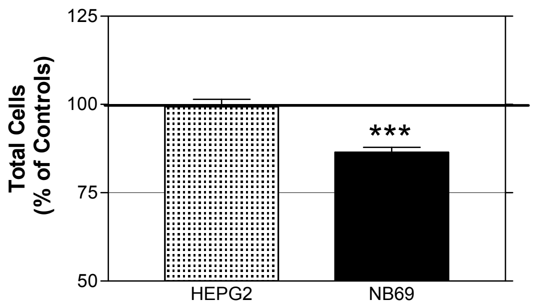

Figure 3. Comparative growth response after 24 h of RF- or sham-exposure. Means ± SEM of a total of 6 (HepG2) and 8 (NB69) independent replicates, with 8 RF and 8 sham dishes per replicate. Normalized data over the total cell number in the corresponding group of samples incubated simultaneously inside the non-stimulated waveguide (sham-exposed). In NB69, the overall effect was statistically significant (p<0.001) with respect to sham-exposed samples.

Cell Growth response to treatments with RF and/or mild hyperthermia

Figure 4 summarizes the cell growth response of the HepG2 and NB69 cancer lines when exposed to the RF signal under conditions of mild hyperthermia (38 ºC). At the end of the 24-h incubation at 38 ºC the sham-exposed samples of both cell lines showed significant increases in total cells (18.8% in HepG2, $p< 0.01$, and 17.9% $p< 0.05$ in NB69) when compared to controls incubated at 37 ºC. Such a temperature-induced effect was not observed when the thermal treatment was applied simultaneously with the RF exposure. When compared to their sham-exposed controls incubated at 38 ºC, the RF-exposed samples kept simultaneously in the same incubator showed significant reduction in the total cell number at the end of the 24-h treatment, both in HepG2 (13.7% below sham, $p<0.01$) and in NB69 (10.1% below sham, $p<0.01$).

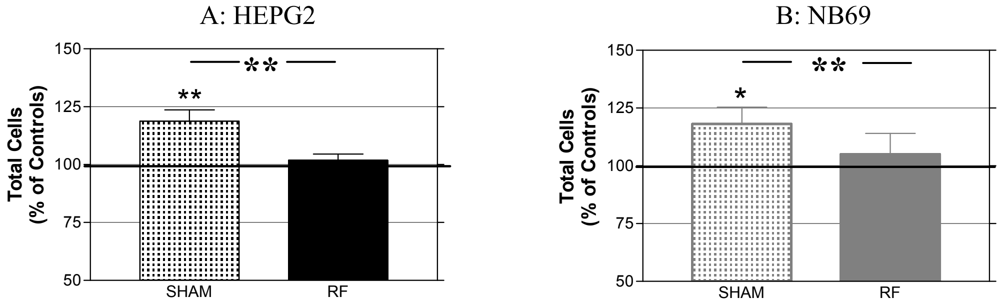

Figure 4. Growth response of HepG2 and NB69 cells after 24 h of simultaneous treatment with mild hyperthermia and RF- or sham-exposure. A total of 5 independent replicates were performed per cell line, with 8 dishes exposed to RF at 38 ºC, 8 sham dishes incubated at 38 ºC and 8 controls growth at 37 ºC, per replicate. Means ± SEM. Data normalized over the total cell number in the corresponding group of controls incubated simultaneously at 37 ºC.

Changes in the kinetics of the cell cycle in response to the RF stimulus

FACS analyses were conducted in order to investigate whether the differential growth responses in HepG2 and NB69 could be due, at least in part, to RF-induced alterations in the cell cycle regulation. No significant changes were observed in the distribution of HepG2 cells in the different phases of the cycle after RF- exposure (data not shown). In contrast, the NB69 line responded to the RF treatment with slight but consistent and statistically significant increases in the percent of cells in G0/G1, both under standard temperature and mild hyperthermia (6% and 3.4 % over controls, respectively, $p < 0.05$; Fig. 5). Also, a significant increase in the percent of cells in G2/M phases (9% over controls, $p < 0.05$) was observed when RF was applied at standard temperature, but not at 38 ºC.

As for the influence of the thermal treatment alone, it induced significant changes in the cell cycle progression of both lines; resulting in shortening of the S-phase in samples incubated at 38 ºC (approximately 30% below controls at 37 ºC, $p < 0.05$). The simultaneous treatment with RF blocks this thermally-induced response, and only small but significant increases in the G0/G1 phases were observed (Fig. 5B).

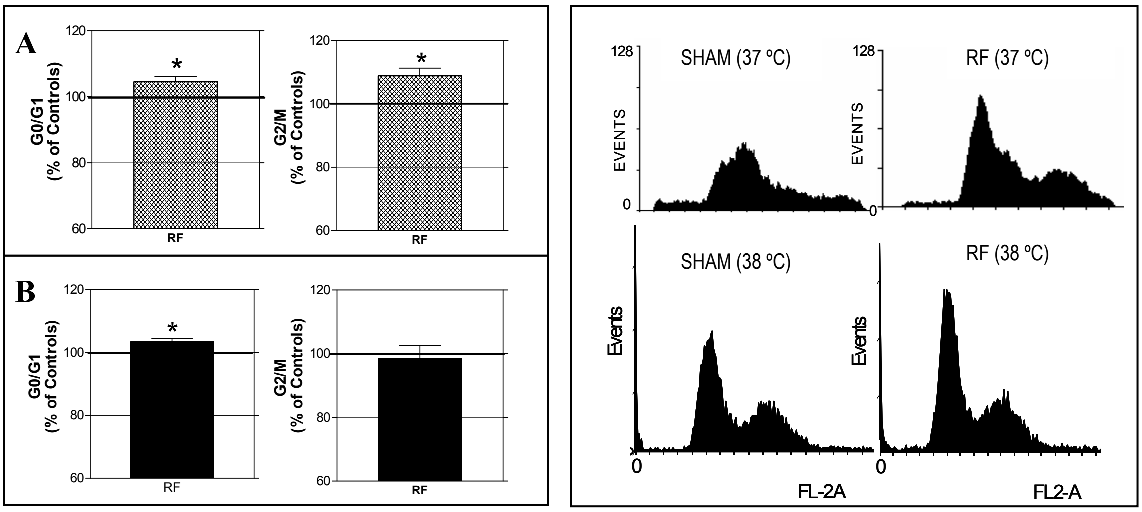

Figure 5. Left: Changes in the percent of NB69 cells in G0/G1 and G2/M phases of the cell cycle in response to RF exposure. A total of 4 independent replicates with 8 RF and 8 Sham dishes per replicate were carried out at (A) standard temperature (37 ºC) and (B) Mild hyperthermia (38 ºC). The data (Means ± SEM) are normalized over the respective sham-exposed samples. Right: Four flow cytometry histograms, representative of RF-exposed and Sham-exposed samples of the line NB69, incubated at 37 ºC or 38 ºC.

Discussion

The biological effects of low power or short-pulse RF signals that do not induce significant hyperthermia in the exposed tissues have not been investigated sufficiently. A more complete knowledge of the non thermal or subthermal effects of the RF radiation on biological systems is of utmost interest from two biomedical points of view. On the one hand, an increasing number of medical applications based on RF treatments have been developed in recent years. A better understanding of the biological responses to RF involving phenomena other than thermal could be useful to the development of new treatments, including co adjuvant therapies in oncology, traumatology or pain relieving, among others. Furthermore, it is widely accepted that hyperthermia can enhance the sensitivity of cells to radiation and drugs, and mild hyperthermia (by 1–2 °C) has been reported to induce heat-shock proteins, increase biophylaxis and immunocompetence, prevent stress and fatigue, and reduce depression or anxiety, which could contribute to diminish adverse reactions to chemotherapy and potentiate its antitumor effects (Skitzki et al., 2009; Yamada et al., 2009).

On the other hand, the level of exposure to environmental RF emissions has progressively increased in developed countries. A positive correlation between RF exposure and tumorigenesis has been suggested by a number of epidemiological studies (Hardell et al., 2008; Sadetzki et al., 2008; Khurana et al., 2009). These results have received limited support from experimental data indicating that RF fields can induce DNA breaks (Garaj-Vrhovac and Orescanin, 2009), chromosome aberration (Mazor et al., 2008), as well as alteration of gene expression (Remondini et al., 2006; Zhang et al., 2008). Despite of the fact that these in vivo and in vitro results could be indicative of possible damaging effects of RF fields, other experimental results do not support such a possibility. Thus, whether or not the reported biological responses may be induced through subthermal phenomena, is presently a controversial issue that needs to be elucidated.

Altered cell proliferation is among the most sensitive phenomena currently used to study the cellular response to environmental carcinogens. However, the available evidence on RF effects on cell proliferation is scarce and the results are conflicting (Higashicubo et al., 2001; Pérez-Castejón et al., 2009). The present study addresses the hypothesis that RF signals at subthermal doses could influence cancer progression by increasing or accelerating cell proliferation in two human cancer cell lines. We examined cell proliferation following exposure to RF radiation at standard incubation temperature (37 ºC) or at mild hyperthermia (38 ºC), and analyzed comparatively the cell responses induced by a 2.2-GHz pulse-modulated, S-band radar-like RF signal with high instantaneous amplitude and very low average power, and by a 1 ºC hyperthermia caused by the corresponding increase of the incubation temperature.

In the NB69 line the RF treatment at standard temperature resulted in significantly decreased cell number (13.5% below sham-exposed samples), accompanied with significantly increased proportions of cells in the phases G0/G1 and G2/M of the cell cycle. Also, a modest but consistent and statistically significant increase in the rate of necrosis (2% over sham) was observed in the NB69 line; however, this subtle cytotoxic effect would have little impact on the overall cell growth rate. The other human cancer line tested, HepG2, did not respond to the 24-h exposure to the same RF treatment when it was applied at standard temperature of 37 ºC. However, under +1 ºC hyperthermia, which induced significantly increased cell growth in sham-exposed NB69 and HepG2 cultures (about 18% over control samples at 37 ºC), both cell lines responded to the RF signal with significant ($p < 0.01$) reductions in cell growth, (10.1 % below sham-exposed in NB69 and 13.7 % in HepG2). In NB69 this RF-induced reduction in cell growth at 38 ºC was accompanied with a modest, though significant increase in the fraction of cells in phases G0/G1.

A similar RF effect on cell proliferation was observed by Velizarov et al. (1999) in transformed human epithelial amniotic cells exposed to a 960 MHz microwave radiation. These authors reported that at incubation temperature of 39 ºC a significant reduction in cell proliferation occurred in the exposed cells when compared to non-exposed (control) samples. However, in contrast to our results, the treatment with mild hyperthermia alone did not change significantly the proliferation of the amniotic cells with respect to control samples incubated at 37 ºC. Taken together, the results of both studies indicate that, when administered alone, mild hyperthermia induces different responses in different human cell types; whereas exposure to subthermal doses of RF signals in the GHz range could elicit a common, antiproliferative response in different, thermally stimulated cell lines.

Additionally, in both NB69 and HepG2 cell lines the RF treatment neutralized the thermally-induced proliferative response observed after incubation at 38 ºC. This result could explain the apparent lack of response reported by other authors in cells exposed to relative high, thermal doses of RF radiation (see, for instance, Takashima et al., 2006). It is possible that in some of those studies a mild thermal effect had occurred in fact, that would be counterbalanced by an electromagnetically-induced response. In other words, the thermal electromagnetic signal would have induced two opposite, simultaneous responses resulting in a null or non detectable overall effect.

In conclusion, a 24-h treatment with subthermal doses of 2.2 GHz, pulse-modulated RF radiation elicited different responses in two human cancer cell lines. The NB69 line was proven responsive to the RF stimulus, exhibiting significant reduction in the number of cells, both under standard incubation temperature (37 ºC) and under mild hyperthermia (38ºC). Such antiproliferative effect was associated to cell cycle alterations. The HepG2 cell line was not responsive to the RF signal when applied at standard temperature conditions. However, at a temperature of 38 ºC, the RF stimulus induced in HepG2 an antiproliferative response similar to that in NB69, the cultures reaching growth rates equivalent to those of controls incubated at 37 ºC. Additionally, the thermal treatment alone induced significant shortening of the S-phase in both lines, which resulted in significant acceleration in the cell cycle progression and increased cell number when compared to samples incubated at 37 ºC. The simultaneous treatment with RF neutralized this thermally-induced response, indicating that the electromagnetic and the thermal stimuli might exert opposite effects on cell proliferation and cell cycle progression. As a whole, the antiproliferative responses elicited in two different human cancer cell lines are not supportive of the hypothesis that repeated exposure to weak, RF electromagnetic signals in the GHz range can exert carcinogenic effects on transformed or initiated human cells. Further research would be necessary in order to elucidate whether or not the described, RF-induced cytostatic effects might be relevant to the potential development of emerging, electromagnetic-based therapeutic strategies.

Acknowledgment

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Exposure of the French population to 50 Hz magnetic fields: EXPERS study

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Abstract
To study the exposure of the French population to 50 Hz magnetic fields (MF), two samples (children and adults) representative of this population were created. Each person wore an EMDEX II measuring and recording the MF to which he/she was exposed during 24h, and has progressively filled in a timetable and a questionnaire with information about themselves and their homes. When returning the meter, the pollster recorded the GPS coordinates of their homes.

In total, 978 series of MF were validated for children and 1054 for adults. The arithmetic and geometric means observed were respectively 0.09 and 0.02 µT for children and 0.14 and 0.03 µT for adults.

Introduction
The magnetic field (MF) at extremely low frequency (ELF) have been suspected, for around 30 years, to be responsible for several pathologies in humans, more precisely, childhood leukemia (Wertheimer et al., 1979). In 2001, the International Agency for Research on Cancer (IARC) classified ELF MF in the category II-B (“possibly carcinogenic to human“).

The last collective assessment by international expert groups (WHO 2007, SCENHIR 2009) concluded that the last major questioning concerning ELF MF is the statistic correlation observed in several meta-analysis between the increase of childhood leukemia risk and a MF exposure higher that 0.4µT in means over 24h (Ahlbom et al., 2000), without any causal relation.

The exposure of the French population to these types of fields is known only very approximately. In 2007 the Health Ministry initiated a study about the exposure to 50 Hz MF of a representative sample of the French population (1000 children from 0 to 14 years and 1000 adults of 15 years and over). We present here the results of this study called “EXPERS” for EXposure of the PERSson.

Material and methods

Recruitment of the volunteers

One of the problematics linked to this study was to create a sample of 1000 children and 1000 adults based on random sampling method. For this a call for tender was launched and MV2 Conseil was chosen to conduct this work and collect the data.

This phase of data collection was conducted in 3 campaigns (February-April 2007, October 2007-April 2008 and October 2008-January 2009).

MV2 created a database made up of a file with 95 362 phone numbers taken in a totally random way from the general file of phone numbers attributed in France, except professional phone numbers. The selection of individuals was based on these numbers, respecting the distribution of the population in the 22 regions[1] of metropolitan France according to the 2006 census (www.insee.fr).

Data collection

Each volunteer recruited wore an EMDEX II (Enertech, USA) measuring and recording every 3 seconds the 40-800 Hz MF during 24h. Figure 1 gives an example of measurements recorded by a volunteer.

Among the equivalent models on the market, we chose this meter because it enables the distinction between the 50 Hz component and the harmonics, which is useful in analysing the different sources of MF. Moreover, we have checked that it was not disturbed by electromagnetic fields emitted by GSM. (Magne et al., 2006).

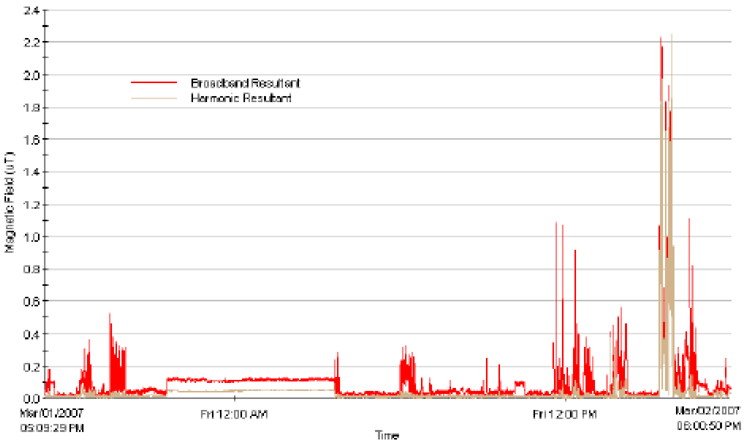

Figure 1. example of MF record for a volunteer.

Each volunteer progressively completed a timetable in which he noted his activities, with starting and ending time, the location and the electric appliances used.

When returning the meter, the pollster filled in with the help of the volunteer a questionnaire containing information relative to the volunteer (age, sex, profession, …), his home (year built, number of years spent in the home, number of people living in the home, energy type, heating method of home and water, …)

[1] France is divided into 22 regions and 96 departments.

He also noted the GPS coordinates at the volunteer's home front door. These coordinates were transmitted to ERDF (the French electricity distribution network operator) and RTE (the French electricity transport network operator) in order to identify all the electric networks close to each home. The criteria of identification of electric networks around homes are given in another communication (Magne et al., 2010). The results given here concern overhead and underground high voltage networks, from 63 to 400 kV, and the electrified train networks (data June 2009).

Description of the database

The number of volunteers having participated in the MF measurements was 2 148 (2.25 % of the phone numbers called). In total, the information relative to 2 048 people (989 children and 1 059 adults) was validated by MV2 Conseil.

When looking at the distribution of the database created, we notice that 11 departments out of 96 are not represented (note that we did not fix any quota per department).

After checking the compatibility of MF series and timetables, 16 series were deleted. The sample analysed was composed of 978 children and 1054 adults.

Results

Descriptive analysis

The arithmetic means (MA) and geometric means (MG) observed are respectively 0.09 and 0.02 µT for children and 0.14 and 0.03 µT for adults. Figure 2 gives the distribution of MA for both populations.

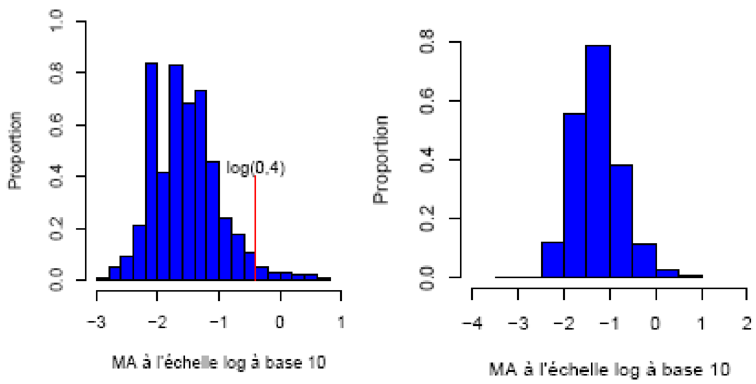

Figure 2. distribution of MA over 24h (children/adults).

On the whole, 3.1% of children observed an arithmetic mean higher than 0.4 µT. Two of them observed a geometric mean higher than this value.

When considering the exposures outside the period of sleep, the mean exposures for children are 0.05µT (MA) and 0.02 µT (MG). Eleven children (1.1%) have recorded a MA higher than 0.4 µT.

The mean exposure for adults are 0.10 µT (MA) and 0.03 µT (MG).

A comparison of mean exposures was performed for both populations with the help of rank tests. Figure 3 gives an example.

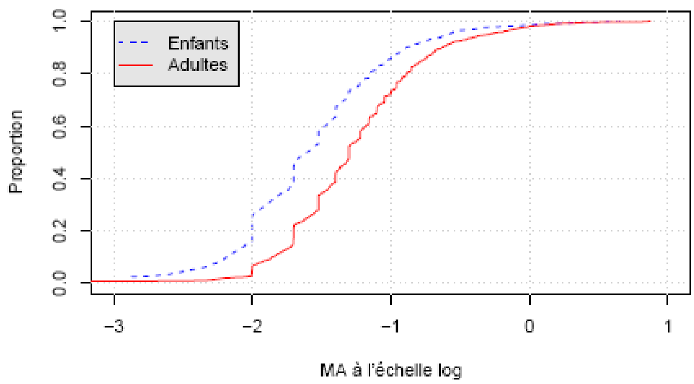

Figure 3. distribution function of 24h MA for children and adults.

The results show that:

– children are less exposed than adults,
– children are more exposed at home than outside, while it is the opposite for adults,
– at home, both populations are more exposed during the day than during the night (it is the opposite for adults in MG),
– regarding electric networks:
  - o for both populations, the mean exposure (at home and over 24h) are higher for the volunteers living close to electric networks than for those living far away from these networks,
  - o the MA (at home and over 24h) are not different for children living close to high voltage networks and for those living close to train networks,
  - o the MG at home (with and without sleep period) are higher for children living close to high voltage networks than for those living close to train networks (it is the opposite for MG over 24h),
  - o the MA and the MG (at home and over 24h) are not different for adults living close to high voltage networks and for those living close to train networks,
– people living in Ile-de-France are more exposed than in the other regions.

Characterization of the exposures

We are seeking to characterize the mean exposures in function of the data collected. A study on the data of the first phase has shown that there exists relationships of dependence between the mean exposures and some explicative variables. In order to characterize theses structures, we chose firstly linear models. These models gave very low levels of explained variance. This can be explained by the fact that the studied variables are not the only ones to influence the exposure, or by the fact that the relationship is not linear. For further analysis, we thus decided to use non parametric multidimensional models.

The factors identified as influencing the mean exposure are:

– the age,
– the density of population of the department,
– to have placed the EMDEX II close to a clock radio (for 24h exposure),
– living in a city of more than 2 000 inhabitants,
– living in a building,
– the presence close to the home of overhead power lines or of electric train networks,
– the time spent on a computer,
– the time spent in shopping centres,
– the time spent on train transports,
– the time spend in non-electric transport,
– the time spent at school.

All are not factors influencing both populations, nor both means, nor exposure over 24h and outside period of sleep.

The level of variance explained remains very low (between 10 and 30 %). The models obtained are thus non predictive.

Search of exposure classes

We are seeking to separate the population studied in several classes, by regrouping those who have the most similar exposures. Each series of MF is described by 7 indicators: maximum value, 3rd quartile, MA, MG, median, standard deviation and RCMS (Rate Change of Metric Standardized, indicator measuring the temporal variability of the signal). A hierarchic classification is then applied on these indicators centered and reduced.

Figure 4 gives an example of dendogram of classification. For each population and each scenario (24h or outside period of sleep), we chose 3 classes of exposure.

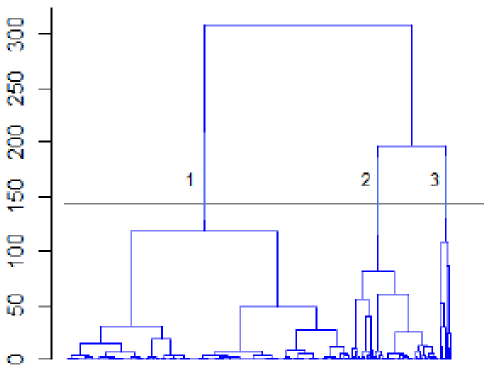

Figure 4. example of classification (exposition aver 24h for adults).

After we used a logistic regression in order to identify the variables leading a subject to belong to the most exposed class. The results depend on the scenario, type of mean and population considered.

The main factors which increase the probability to belong to the most exposed classes are:

- to have placed the EMDEX II close to a clock radio (for 24h exposure),
- the presence close to the home of overhead power lines or of electric train networks,
- living in a city of more than 2 000 inhabitants and the density of population of the department (for adults),
- the time spent on train transports,
- the time spent in shopping centres (for adults).

The main factors which decrease the probability to belong to the most exposed classes are:

- the time spent in non-electric transport,
- the time spent at school.

Discussion

The mean time to recruit one volunteer was 70 minutes. The recruitment of children was even more difficult than those of adults. This led to modifying the recruitment protocol by privileging children from the second campaign.

Tests of homogeneity have been performed in the 11 departments without subjects comparing to the corresponding regions: we looked at if the probability of selecting an individual in these departments is the same as the probability of selecting an individual in the corresponding regions. The statistical tests show that the fact of having no volunteers in these 11 departments is completely by chance.

One the one hand, the analysis of volunteer profiles does not show any difference in the ratio boy/girl in the children compared to the French population. On the other hand, women are more represented than men in our sample. In the same way, the profile of ages show a deficit of children under 6 years of age, and a surplus of 35 to 50 year old adults. This can be explained by the modification of recruitment protocol: we suggested to the adult to record the measurements at the same time as the child, often it was probably the mother who accepted.

On the whole, 3.1% of children observed an arithmetic mean higher than 0.4 µT. Two of them observed a geometric mean higher than this value. These percentages are higher than what is given in the literature, that is why we have tried to explain these high exposures. This phenomena has appeared during the first measurement campaign. We have then noticed that the high exposures corresponded to signals with values which were sometimes high (several µT) and constant during the night, and a ratio of harmonics around 1/3. These signals corresponded to magnetic fields emitted close to clock radios. Additional investigations into clock radios have shown that:

- the MF level vary strongly from one model to another,
- the MF source is the transformer, which is located in the clock radio or deported in the socket,
- the level of MF decrease very rapidly with the distance,
- at 50 cm, the magnetic field emitted by the clock radio is negligible.

So the highest 24h measurements can be explained by the presence of clock radios during the night. But are these measurements representative of the exposure of the person? In order to avoid measuring MF in contact with clock radios, we asked in the following campaigns to respect a distance of 50 cm between the EMDEX II and any electric appliances during the night, and we asked the volunteers whether they had respected this requirement. All did not do it!

When considering the exposures outside the period of sleep, 11 children (1.1%) have recorded a MA higher than 0.4 µT. This result is coherent with the literature.

The 24h measurements may thus include a measurement bias which overestimates the exposure. That is why we studied the exposure over 24h and the exposure outside the period of sleep.

Conclusions

Beyond the difficulties encountered by MV2 Conseil to perform the measurements, we can remember that 3.1% of the children have observed an arithmetic mean higher than 0.4 µT. The main exposure sources for these high exposures are clock radio (the real exposure of the person was overestimated). When looking at the exposures outside the time of sleep, 1.1% of children have observed an arithmetic mean higher than 0.4 µT. This value is consistent with the literature.

Children are less exposed than adults. An explanation could be the fact that they move less during school periods.

With the descriptors calculated on the series, each type of population is divided in 3 classes of exposure. The factors identified in terms of higher means or belonging to most exposed classes are mainly having put the EMDEX II close to a clock radio, having his home close to overhead power lines or to electric train networks, the time spent on train transports, in commercial centres, on a computer or watching television, living in a city of more than 2 000 inhabitants or in a building. These factors depend on the population considered (adult or children), the type of mean (arithmetic or geometric), and the scenario (over 24h or outside period of sleep).

The analysis of mean exposures has shown than the variables retained do not alone allow to characterize these means.

The work presented here will be continued by including the presence or not of distribution lines and substations. This information could improve the characterization of mean exposures in terms of explained variance.

Another possible use of these data is the validation of physical models of assessment of magnetic fields.

Acknowledgment

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Impact of Post-Processing in human body dosimetry exposed to 50 Hz magnetic field

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Abstract

In order to comply with the requirements on the exposure of workers to electromagnetic fields, numerical simulation is necessary because the currents induced in the body are very difficult to measure. Induced currents are computed by solving Maxwell equations by means of different numerical methods (FEM, BEM, FIT, etc...) operated on a panel of models of human body which are available with variable geometrical sharpness. To be able to compare the numerical accuracy of these models, we need to understand, for each numerical method, the impact of the quality of the meshing on the reliability of the maximal computed value of the induced current.

In this study, we apply four quality criteria on four types of methods working in the ELF domain, applied to one single mesh offering medium sharpness. By analyzing the maximal induced currents in a particular exposure case to vertical induction, we found that the efficiency of our criteria is highly dependent on the method of resolution in parts of the body which are too coarsely meshed.

Introduction

The European Directive 2004/40/CE dealing with electromagnetic fields for workers defines two reference values: the AV (Action Value) which is a warning threshold, and the ELV (Exposure Limit Value) which have not to be exceeded for biological reasons. We can compare both values via simple models such as on Fig. 1.

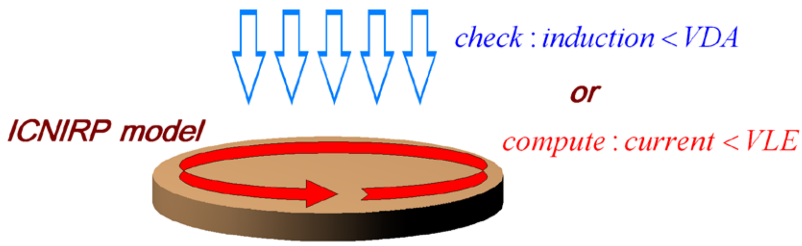


Fig. 1. Simple ICNIRP exposure model illustrating AV and ELV.

The magnetic and electric field can be easily measured *in situ* and then compared with the AV which is 500μT at 50Hz for the magnetic induction and 10 kV/m for the electric field, while the ELV corresponds to the RMS value of the current density averaged over 1 cm^2 surface normal to the current vector, and is considered only in the CNS (Central Nervous System). To evaluate such a value inside the body, and compare it to the 10 mA/m^2 threshold, not only a numerical simulation is required, but the computation must ensure reliable results all over the CNS organs, which depends on the association of a robust resolution method and a anatomically realistic modelling of the body (Ducreux et al 2009).

The numerical methods to solve Maxwell equations in ELF domain

In order to so solve the Maxwell equations for the induced currents in the human body at 50 Hz, we considered four different formulations : two of them are general purpose FEM (Finite Element Method) for industrial applications of the QSA domain (Quasi-Static Approximation), the third one is a dedicated method derived from the first one, and the last one is derived from the FIT (Finite Integration Technique).

Formulation 1: general purpose magnetic FEM “A-Phi”

The unknowns are the magnetic vector potential $\mathbf{A}$ in the entire space and the scalar electric potential φ in the body. The computer code we used for that formulation is *Code_Carmel3D* (Henneron et al. 2007), which is well fitted to magnetic hysteretic media in electrical machines accounting rotation and circuit coupling. That method is the most ancient and the most practised in ELF domain of electrotechnics.

Formulation 2: general purpose electric FEM “T-Omega”

The unknowns are the electric vector potential $\mathbf{T}$ in the body and the scalar electric potential Ω in the whole space. The tools we have selected for that formulation are *Code_Carmel3D* and Maxwell3D (Miller et al. 2008). That second method is comparable with the first one, while in this context it seems to be more accurate, as it ensures strongly the normal continuity of the vector current at interfaces (which is much more interesting than the analogous condition on the magnetic flux density imposed by the A-Phi formulation).

Formulation 3: a human body dedicated magnetic FEM “Phi-A”

In case of human body, the magnetic vector potential $\mathbf{A}$ depends much more on the incident field than on the induced currents. So it may be sufficient to compute the electric scalar potential φ in the body in response to an incident magnetic potential vector $\mathbf{A}$ associated with the incident field, considered as a volume source term. The resulting advantage is a very cheap computation. The code we used for that formulation is an academic one, based on the library Getfem++ (Renard et al 2010).

Formulation 4: a « FEM-like » Finite Integration Technique

Generally, the FIT is devoted to the high frequency domain, because it solves the complete Maxwell equations, and moreover it can work directly with short wavelengths on the high resolution voxel-phantoms. Recently, this method was made usable with linear tetrahedrons, within non-structured meshes, by running the CST-EM Studio code

(Weiland et al 2008), and in addition, a low frequency domain solver is now proposed, so that the FIT can easily compete in our human body ELF benchmark.

Benchmarking our formulations on a simple meshing test case

First we compared the formulations on a very simple problem, i.e. an non-magnetic ellipsoïd with an homogeneous conductivity of 0.2 S/m, subjected to an uniform 50Hz incident magnetic induction of 500µT directed along the small axis shown on Fig.2.

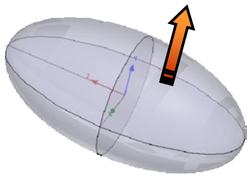


Fig. 2. Configuration of the test.

For such a system, we easily obtain the following analytical expression of the maximal current $J_{\max}$:

$$J_{\max} = \omega B \frac{ab^2}{a^2 + b^2}$$

Where a and b are the major axes, B is induction and ω its angular frequency. Then we can evaluate the impact of the mesh refinement on the local maximal value of the induced current computed with the four formulations. For that purpose, we treated different axis dimensions for the two types of meshes of Fig. 3.

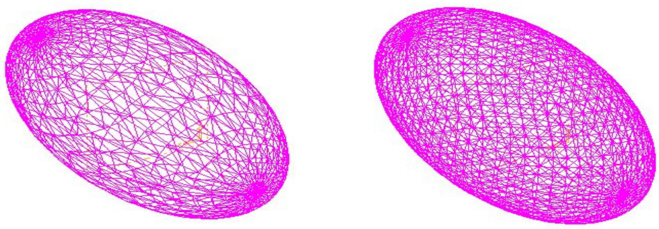


Fig. 3. Coarse mesh (3000 tetras) and fine mesh (15000 tetras).

As we can see on Table 1, the refinement of the mesh fit the formulations when they are of the same family (i.e. 1 with 4 and 2 with 3) but it cannot make all the four formulations converge to the exact result.

Table 1. Maximum induced current density (mA/m^2) : case of the 60x30 cm ellipsoid.

	Formulation	Coarse mesh	Fine mesh
1)	Carmel ($A-\varphi$)	8.29	5.30
2)	Carmel ($T-\Omega$)	5.46	5.18
	Maxwell3D ($T-\Omega$)	4.87	5.18
3)	Getfem++ ($\varphi - A$)	7.50	5.30
4)	CST (FIT)	6.04	5.19
Analytical solution		**5.30**	

Benchmarking our formulations on a particular human body model

The « formulation sensitivity » that we found in the above elementary test is much more significant on a realistic human body mesh such as shown on Fig. 4.

Fig. 4. Studied human body mesh (provided by Ansoft).

This model contains around 100000 tetras (70% for the body) and 21 organs for which we can see on Fig. 5 that their size, shape and conductivity are ill-assorted.

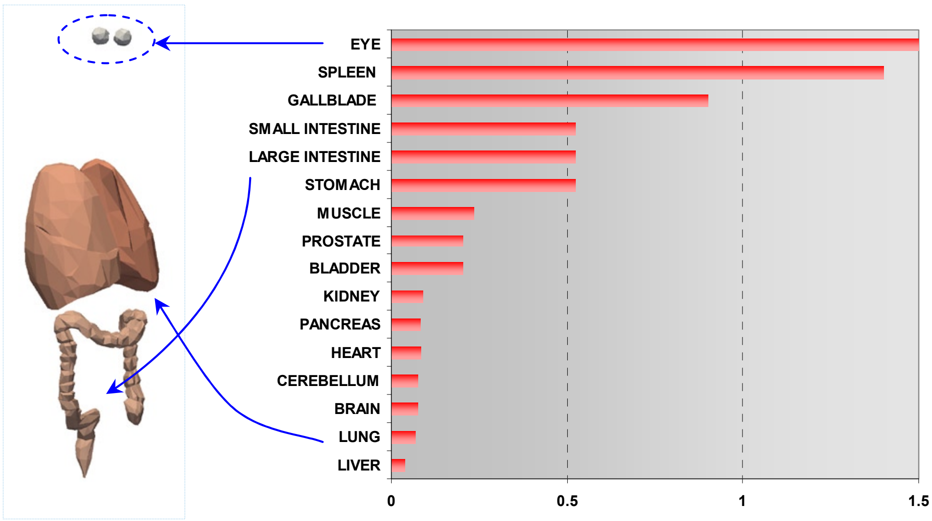


Fig. 5. Some components of the human body model and their conductivity (S/m).

Assuming a uniform vertical incident field of $1\,\mu T$ at $50Hz$, we computed the maximal induced current in each organ obtained by the four formulations. The results show important discrepancies (see "EYE" on Fig. 6), which are not located into the high conductivity organs only (see "PROSTATE" and "PANCREAS" on Fig. 6). In all the conductive organs, the two general purpose formulations 1 and 2 are relatively close together compared to the derived formulations 3 and 4. Nevertheless, Fig. 6 shows that formulation 1 and 2 differ in the muscle, that suggest some meshing effect (muscle has a complex shape because it is defined as the whole body less all other organs).

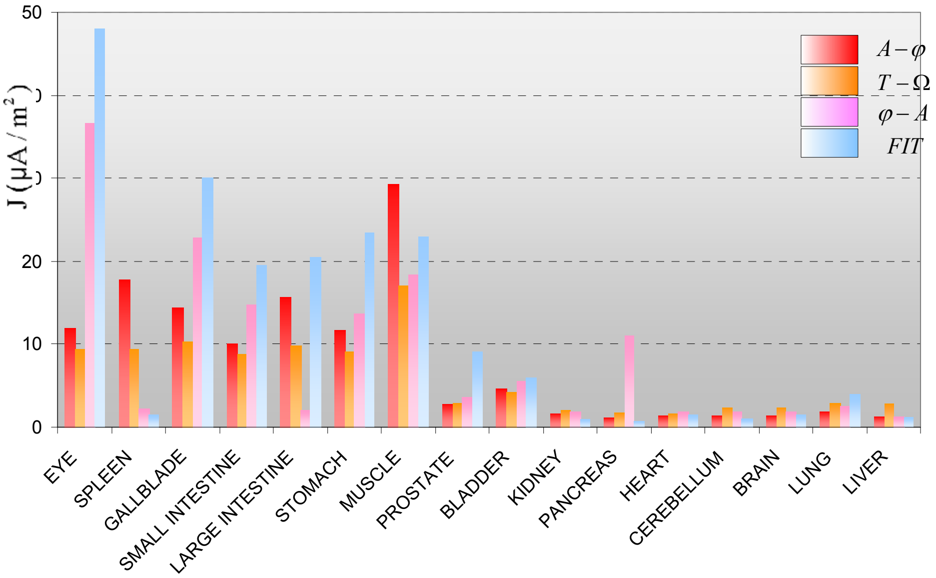


Fig. 6. Maximum induced current density in organs.

Post-processing of the results using mesh quality criteria

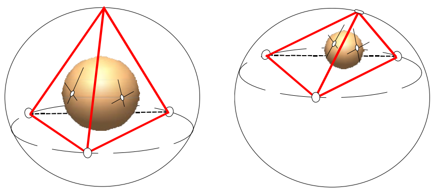
In order to quantify the impact of the mesh quality and of the formulation on the reliability of the maximum computed current, we can use local error estimators. As the computation provides one current value for each tetrahedron, we associate the local error with a so called "quality criterion" assigned to each tetrahedron, which can be estimated "a priori" or "a posteriori" (i.e. before or after the computation) – see table 2.

Table 2. "A priori" and "a posteriori" error estimators.

Error estimator	a priori	a posteriori
mesh dependant	geometrical	statistical
formulation dependant	spectral	energetical

A priori geometrical criterion

This very well known criterion is based on the shape of the tetrahedron. It is build with the ratio of the radius of in-sphere R_{int} to the radius of circumscribed sphere R_{ext} as shown in Fig. 7. So the quality q is unity for an equilateral tetrahedron and is zero for a flat one (*sliver*).



$$q = 3\frac{R_{int}}{R_{ext}}$$

Fig. 7. Example of a "good" and of a "bad" tetrahedral geometry

A priori spectral criterion

This criterion is based on the numerical conditioning of the elementary matrix. In that sense, it includes some physical properties of the problem, such as the static or dynamic nature of the magnetic response. Hereafter the elementary matrix for the $A-\varphi$ formulation is considered (the dynamic term is the one which depends on the skin depth δ). N_A and N_φ are respectively the edge and nodal shape functions for tetrahedra:

$$\mu M(\delta) = \begin{bmatrix} (rotN_A)^2 & 0 \\ 0 & 0 \end{bmatrix} + \frac{i}{\delta^2} \begin{bmatrix} N_A{}^2 & \frac{1}{i\omega} N_A^T gradN_\varphi \\ \frac{1}{i\omega} gradN_\varphi^T N_A & \frac{1}{\omega^2}(gradN_\varphi)^2 \end{bmatrix}$$

Once the above matrices are gauged, we easily compute the non-zero eigenvalues (there are 3 non-zero eigenvalues for the first static matrix and 6 for the second dynamic matrix). Then we deduce the condition number ρ and draw the static and dynamic quality criteria q by the following classical form :

$$q = 1 - \left(\frac{\sqrt{\rho} - 1}{\sqrt{\rho} + 1} \right)^2$$

We found that for the $A-\varphi$ formulation, the static and dynamic criteria are very similar except for very large distortions for which the static criterion is slightly more selective. Moreover, after a scaling of 30% accounting that “perfect regular” shape is equilateral for geometrical quality and rectangular isosceles for spectral quality, one observes (Fig. 8) that both “a priori” criteria are quite similar. This fact can be explained by arguing that for flat elements have a nearly singular jacobian matrix, which is used for computing the derivatives of shape functions. Therefore, the more the jacobian matrix is close to be singular, the more the resulting elementary matrix will be ill-conditioned.

Fig. 8. Bad elements selected by “a priori” criteria : geometrical (a), spectral (b) for the A-Phi formulation.

A posteriori statistical criterion

This criterion is based on the distribution of the values computed for the entire mesh. Generally, it can be assumed that the few last percentiles of the distribution are non-significant because these extreme values are due to a poor numerical behaviour of the badly shaped elements. This very simple approach works in most cases.

As expected, the rejected poor elements depend on the formulation. The Fig. 9 compares the last deciles of the current obtained with both general formulations $A-\varphi$ and $T-\Omega$, and exhibits an exploding divergence for the last 2%, what implies that aberrant elements are sensitive to the formulation : on Fig. 10 (a), the tetrahedrons filtered with $A-\varphi$ are mainly located in the interior of the body, so they are supposed to be bad elements, while on Fig. 10 (b) the same filtering with $T-\Omega$ eliminates some tetras on the surface of the trunk, although they seem to be "true" high current elements.

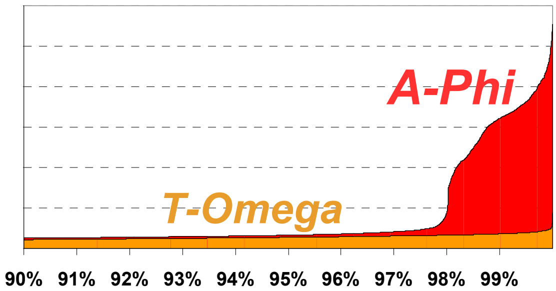


Fig. 9. Diverging last decile of currents distribution.

A posteriori energetical criterion

This criterion is based on the detailed comparison of both general formulations $A-\varphi$ and $T-\Omega$, which are supposed to bound the exact solution (Ren et al, 2002). A measure of the distance between both solutions may be evaluated for each tetrahedron via some energetic normalisation of the residue of constitutive laws, either conductive or magnetic, such as defined in last column of Table 3.

Table 3. Combination of solutions for the constitutive law checking.

formulationr	solution field	derived field	constitutive law
$A-\varphi$	$B_{A-\varphi} = rot\,A$	$E_{A-\varphi} = -i\omega A - grad\varphi$	$J_{T-\Omega} = \sigma E_{A-\varphi}$
$T-\Omega$	$J_{T-\Omega} = rot\,T$	$H_{T-\Omega} = T - grad\Omega$	$B_{A-\varphi} = \mu H_{T-\Omega}$

We can adjust that norm so that the quality criterion on each element returns unity if the residue is null and returns zero if the relative residue is for instance more than 100%. We found the second criterion (magnetic law) is unity in the whole body, what justifies the basic hypothesis of the $\varphi - A$ formulation, i.e. scattered induction is negligible before the incident one. Moreover, we can note on Fig. 10 (c) that the first criterion (conduction law) is much more selective than the statistic criterion, what indicates that both "a posteriori" criteria are far to be equivalent.

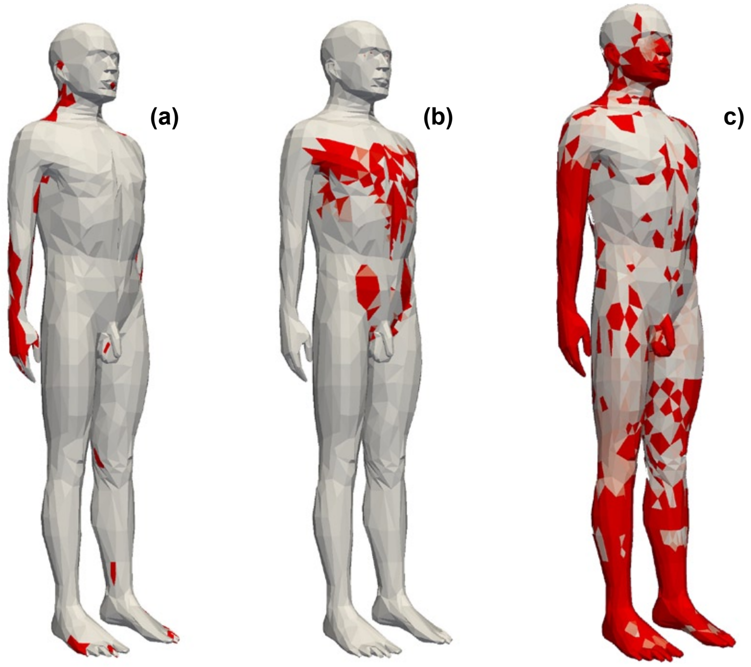


Fig. 10. Bad tetrahedrons selected by our "a posteriori" criteria : statistical A-Phi (a), statistical T-Omega (b), energetical (c).

As pointed before, the case of the muscle is very particular, since in our computational phantom, it is meshed as the complementary volume of other organs, each of them presenting more or less a convex geometry. Therefore, there are a lot of thin interface layers, such those spotted on Fig. 11. There interfaces are not clearly detected as badly meshed by our "a priori" criteria, but reveal nevertheless a poor "a posteriori" quality, as shown on graph of Fig. 11.

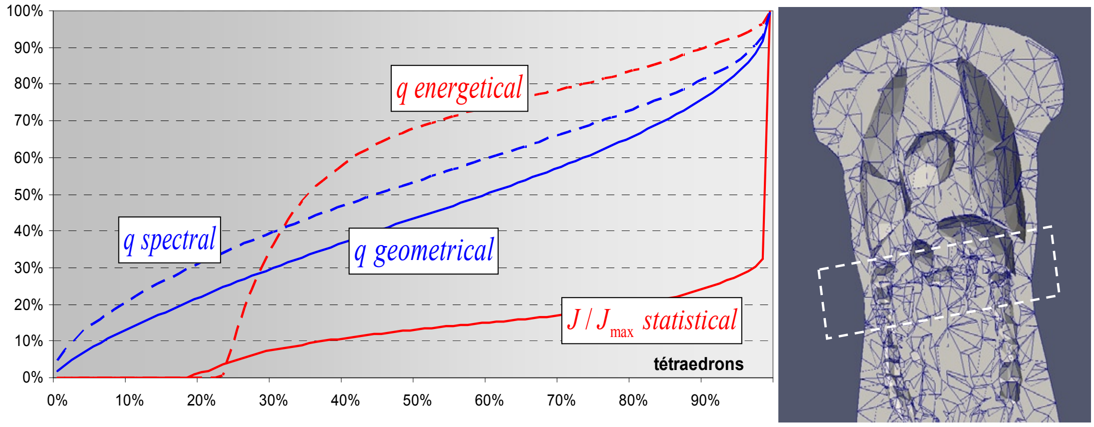


Fig. 11. Case of the "muscle" region. Left : distribution of criteria and right: cut plane in the muscle organ including narrow layers interfacing heart / left lung / intestine / liver / right lung.

Conclusions

Several finite element models of human body and different formulations are available to solve the problem of induced currents by ELF electric and magnetic fields. But till now, there is no general consensus on what combination formulation + mesh is able to provide a reliable maximal current.

We applied four existing formulations on a single human body mesh, two of them working in general purpose codes, the two others being adapted from Maxwell equations to ELF human body configuration. We noticed some discrepancies between results of these formulations, mainly in the high current zones (conductive organs) and in the badly meshed parts of the model.

Then, we defined four quality criteria in order to post-process these results, two of them so-called “a priori” depending on the mesh and the two others called “a posteriori” depending on the results. We found that the “a priori” criteria detect the bad shaped elements but not the high current elements. The “a posteriori” criteria can detect both the contorted elements and the high currents elements at a time, but they are highly sensitive to the formulation in complex organs such as muscle. For that reason, a mesh refinement should be tried in the inter-organ zones before testing energetical criteria.

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Electric properties of mammalian tissues: ex vivo results from 1 Mhz to 1 GHz

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Abstract
Electromagnetic radiations may interact with biological tissues by the way of biomedical devices for therapeutic or diagnostic purposes (hyperthermia, ablatherapy, NMRI,…). Another situation is related to electromagnetic fields sources in the daily life such as mobile or public or domestic devices. Many studies are currently done to determine their potential effects leading sometime to controversy between the published results. The electric properties of biological tissues are frequency dependence and major parameters that governs these interactions inside the human body.

Techniques for both invasive and non-invasive assessment of tissue characterization were proposed since many decades. Different methods are used to determine them among which the so called bioimpedance.

This paper presents and discuss results of ex vivo measurements on mammalian tissues done less than two hours after excision in a surgery department at the Nancy Cancer Center (France). Dielectric permittivity and electrical conductivity of female breast human tissues in the frequency range from 1 MHz to 1 GHz were measured. They are compared to previously published results and the differences discussed according to the influencing parameters.

Introduction
Interactions between electromagnetic field (EMF) and biological tissue find applications in therapeutic or diagnosis methods. On the other hand, development of devices radiating electromagnetic field, like mobile phone, led to the questions of their possible biological effects. These so called EMF bio-effects have led to controversial models for electromagnetic (EM) dosimetry simulation. One reason is that these models are depending on the knowledge of the electric characteristics of the human body. Electromagnetic properties of biological tissues are thus fundamental parameters necessary for any research in bioelectromagnetics.

Many techniques and methods for measuring the bio impedance exist and are primarily motivated by the frequency band of interest (Burdette & Cain, 1980 ; Foster & Schwan, 1996). Interest in the EM properties of biological tissues began more than one century ago (Schwan & Kay, 1957 ; Foster & Schwan, 1986). Bioimpedance spectroscopy is one of the no-destructive, low-invasive and most promising techniques for biological tissues characterization (Rigaud et al, 1996).

Up to now, the values provided by the literature are not always reliable since these data are sparse and disseminated over the frequency range with great variations even for a same biological organ (Gabriel et al., 1996 ; Surowiec et al., 1985). This is not the only major factor and other parameters had to be taken into account for reliability of the experimental results . Moreover, the measurements taken from a sample are likely to be affected by multiple influencing factors such as the contact with the membrane, the temperature at which the measurement is performed, the pressure on the sample, duration post mortem or the structure of the tissue.

The measures on biological tissue are particular for two reasons : firstly because of variations between the samples under test, on the other hand because of the diversity of influencing factors and the non-availability of references for the sensor calibration (Nadi, 2008). Bio impedance measurements need to compensate for the influencing factors related to biological aspects and those related to metrology and instrumentation. This is a crucial factor at low frequency. The dielectric behaviour of biological tissues is dependent on their nature and on the frequency of interest (Schwan & Kay, 1957). They are deformable, heterogeneous, anisotropic and may be solid or liquid. As example of the parameters influencing the measures, the temperature is one whose effects on the variations of the conductivity and permittivity have been previously investigated and is now well known (Foster & Schwan, 1996 ; Jaspard & Nadi, 2002). Precautions taking account of these influencing parameters are required to ensure metrological reliability of the results by adequate corrections.

Comparative studies remain thus a real challenge. In this paper, ex vivo dielectric data are presented and discussed for female breast tissue.

Material and methods

Measurement cell

The experimental set up is based on a material analyser (HP 4291A). Its measurement cell was modified to allows measurement of small biological samples (Gagny, 1998). Data acquisition is done throught an IEEE connection to a PC. This material analyser works on an original method V/I extended to a large frequency band, up to 1 GHz. The main principle of the cell is similar to the geometry proposed by Von Hippel (Von Hippel, 1954).

The experimental set up and the measurement cell are presented on figure 1 & 2. It is constituted by two circular electrodes of which the upper one could be adjusted throught a precision micrometer. The lower electrode is surrounded by a ring guard and ground planes.

Cell for measuring ex vivo samples

A small support (relative permittivity of 1.1 ; loss tangent δ 0.01) permit to fix the position of the sample on the edge outside the circular lower electrode (Gagny, 1998) in order to cover it completely. According to the cell manufacturer specifications the optimal dimensions of the sample placed in the middle of the measurement cell have a diameter higher than 15 mm and a thickness equal or less than 3 mm. This is one of the technical influencing parameters that could affect the reproducibility but it is not discussed here.

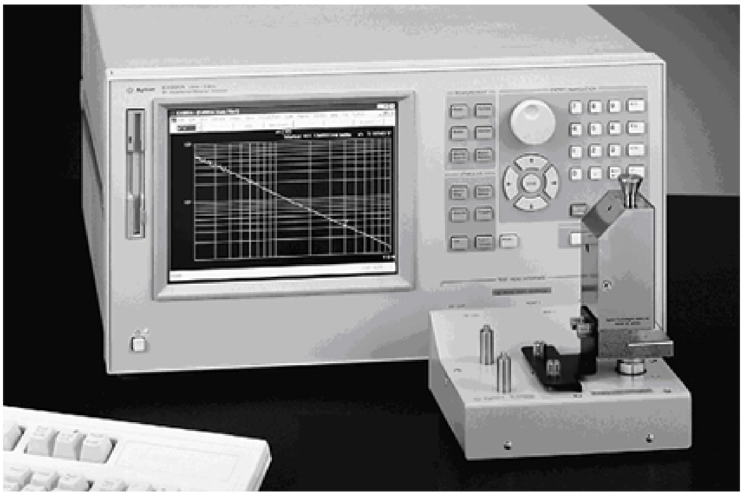

Figure 1.View of the material analyser HP 4291A and the measurement cell.

Eight tissues samples used in this ex vivo study were obtained from surgical ablation procedure on female breast tumor performed in the Cancer Center at the University hospital of Nancy (Gagny, 1998). The samples were excised in tissues surrounding and inside the tumor in the thirty minutes following the surgical procedure by the surgeon. Dimensions of the samples obtained were limited by the clinical constraints since they were given to us on the side to the medical analysis. The necessity to preserve the quality of the tissues excised for biological and medical analysis of the tumor effective excision is one of these constraints. The measurements were performed at ambiant temperature in the maximum of two hours following the surgery, the experimental set up being placed in a room close to the surgery department.

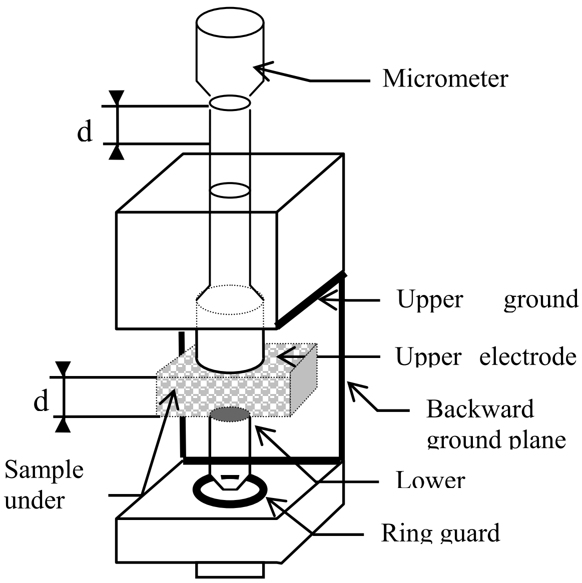

Figure 2. Modified measurement cell for ex vivo electromagnetic characterization.

Method

The instrumentation measures a complex admittance of a 3 points calibrated cell in which the sample is inserted between the two circular electrodes. Theoretical model of the measurement cell allows to solve the inverse problem in order to deduce the permittivity and the conductivity from the measurements. The electric parameters are deduced from the real and imaginary parts of the measure.

$$\varepsilon_r^* = \frac{Y_m^* . d}{j\omega\varepsilon_0 S(1+E_{edges})}$$

where

$E_{edges} = 454 . d^{0.825} . \varepsilon_r^{-0.554}$ is a factor for compensation of edges effect

d : distance between the electrodes [m]
ε_r^* : complex permittivity
Y_m^* : complex admittance

ω : pulsation [rad/s]
ε_0: vaccum or air permittivity
S : surface of the circular electrodes [m^2]

In the low frequency band, one must take account of major influencing parameters such as the well known phenomena of electrodes polarization (Foster & Schwan, 1986). Other metrological parameters like the difficulty to calibrate the measurement cell, the variations of biological parameters such as the anisotropy and heteregoneity of the samples affect the reproducibility of the results.

One advantage of the material analyser HP 4291A is that it operates with the V/I procedure extended in a broad band, typically from 1 MHz up to 1 GHz. The automated data acquisition permit to scan this broad band with a logarithmic step giving 201 frequency between 1MHz et 1GHz. All measurements were made between 21 and 25 °C.

Results and discussion

Ex vivo samples

A systematic spectroscopic measurements were done for different samples and compared to the previous results obtained by other authors.The samples were classified according to their nature (muscle, fat) and dimensions. We present below the mean value deduced from measures done on a single sample (mostly non fat) and the mean value for measures on three similar samples with different dimensions and structure (mostly fat).

Measurement of electric conductivity and dielectric permittivity

Among the datas obtained with our method, only the results that could be compared to others for ex vivo human breast are presented on this paper. Measurements for permittivity and conductivity of breast muscle and breast fat samples are presented on figure 3 & 4 and compared to those from Schwan (Schwan & Kay, 1957 ; Stoyes et al.,

1982 ; Foster & Schwan, 1986), Joines (Joines et al., 1994) and Gabriel (Gabriel et al, 1996). One goal is to check the high differences that can be observed between results from one research team to another in the low frequency range.
Concerning our results, as explained above, a spectroscopic logarithmic measures were done between 1 MHz and 1 GHz. For the clarity, the standard deviation is given only for 15 points.

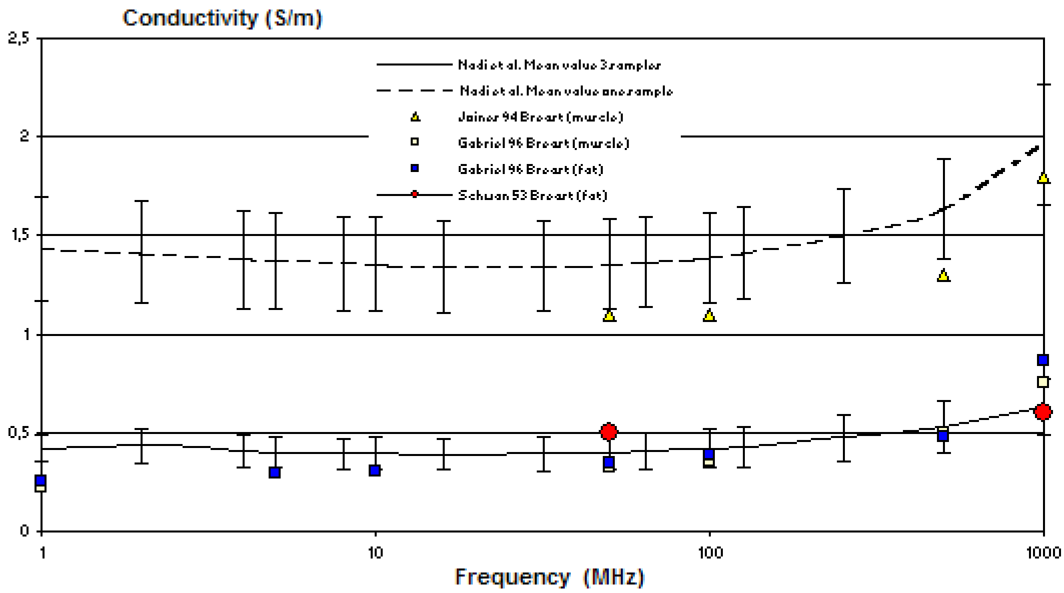

Fig. 3. Electric conductivity of muscle and fat from female breast samples versus frequency compared to previous datas

One can observe that the set of measurements obtained with the mean value from different samples (mostly fatty) is similar to the results given by Schwan (fat) and Gabriel (muscle and fat). However, on can observe that Gabriel's measures on fat and muscle breast are very close. The difference between her datas for fat and muscle are less different than between Joines datas for muscle and her datas for muscle even at high frequency. This is strange and we have no explanation for such high difference.

A mean value was deduced from a set of measures on the same sample (mostly muscle, plain line). The second curve (dashed line) corresponds to the mean value obtained from three different samples and are far from those of Schwan (fat) and Gabriel (muscle and fat). Joines (muscle) datas are also overestimated compared to the other results. However his datas seem similar to our results obtained by mean value on one sample (mostly muscle).

The most important differences for both the conductivity and the permittivity are situated below 10 MHz. It is well known that in this frequency range current conduction through tissue is mainly determined by the tissue structure, i.e. the extra- and intra-cellular compartments and the insulating cell membranes. Thus the nature of the biological tissue is more sensitive at low frequency. On the other hand, the polarizarion effect on the electrodes is also more important below 1 MHz.

Obviously, according to the conditions of both the procedure and the preparation of the sample and its nature, the time after excision, it is normal to find such differences from an author to another.

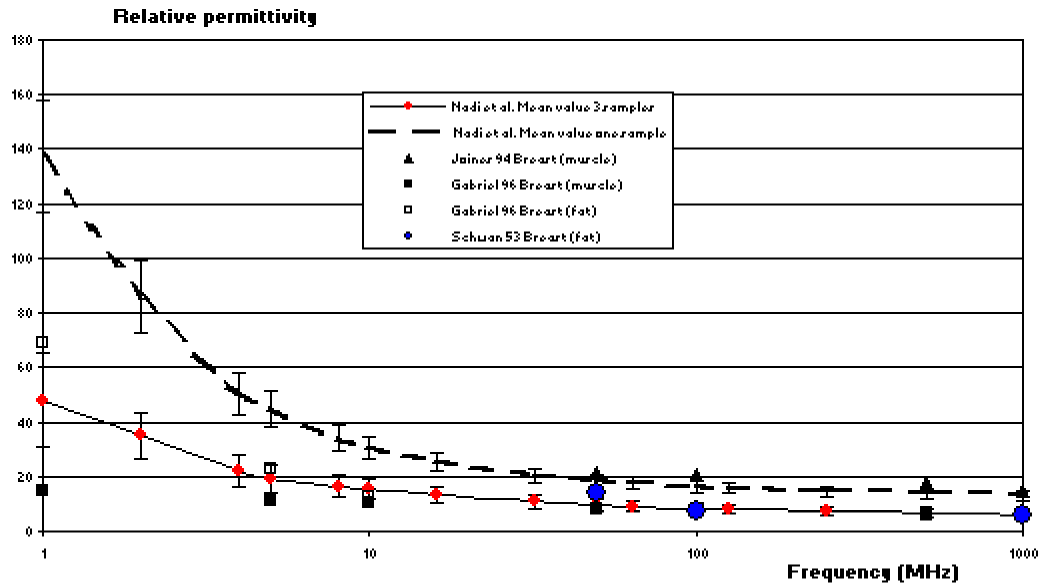

Fig. 4. Dielectric permittivity of muscle and fat from female breast samples versus frequency compared to previous datas

The fact that results are obtained by using different instruments, conditions and procedures (40's up to 80's for Schwan) could explain partly these differences. Schwan used for his early datas manual bridges that did not allow a systematic spectroscopic measurement. This is one reason why some of his first results are sparse and focused on specific frequency. Results from Gabriel were deduced by compilation of datas from the literature and measurements in her laboratory. Joines datas are not overestimated but the differences are certainly due to the nature of the sample used and its preservation after excision. These differences could be by evidence be explained by the importance of fat and muscle heterogeneity of the breast samples and their dimensions that have been used by each author. Over 10 MHz one can accept the hypothesis that all the values are in the same order for the permittivity but this is not true for the conductivity since the difference is greater than 100% between fatty and non fatty breast muscle.

Conclusion

Electric characterization of female breast samples measured ex vivo two hours after the surgery were presented and compared to previous datas. The electrical conductivity and relative permittivity of mammalian human tissues were measured at frequencies from 1 MHz to 1 GHz. The measurements were made using a material analyzer whose measurement cell was adapted to receive small human samples. All measurements were made between 21 and 25 °C.

These results were compared to previous well known datas. Obviously, the differences and variations are due to biological species under test as well as to the metrological difficulties due to the interface between the electrodes and the biological tissue at low frequency.

Metrological parameters affect the reproducibility of the results according to the medium under test and the procedure used by each research team. These differences and variations are due to biological species or organ under test as well as to the metrological difficulties related to the interface between the electrodes and the biological tissue). For mammalian tissues that interest us here, it is necessary to class their heterogeneity as fatty or non fatty since the difference could be over 100% from a sample to another. Other influencing parameters had to be taken into account. Experimental results cannot be rigorously compared as regard to the differences between the natures of the ex vivo sample under test and to the physical and metrological constraints. Comparative studies remain thus a difficult challenge. However, the measurements must stay inside a domain of confidence based on a mean value with standard deviation. At high frequency over 10 MHz, it is possible to admit that the permittivity values are of the same order for fat and muscle breast samples but this is not true for the conductivity.

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Occupational exposure to electromagnetic fields in electrotherapy services and possible related health effects

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Abstract

Aim: The assessment of possible adverse health effects in occupational exposure to electromagnetic fields (EMF) generated by electrotherapy equipments (ETE).

Methods: Exposure evaluation included ergonomical analysis and EMF measurements (static and low-frequency magnetic flux density, low- and high-frequency electric and magnetic strengths). Health status analysis comprised anamnesis, clinical and neurological examinations, exposure and subjective symptoms questionnaires. Psychological tests aim to put in evidence subtle changes of nervous system activity.

Results: 38 electrotherapists vs. 82 matched controls were studied. Magnetic and electric field measured levels generally didn't exceed ICNIRP Guidelines. However, when personnel get closer to the applicators, higher local exposure occurs. Hands and head seem to be the higher exposed. The number of treated patients and the different electrotherapy procedures induce variations in exposure duration. We met three generations of ETE and stray fields seem to be important in older ones. The newer devices show significant lower levels of non-intentional exposure. Health investigations show mainly nervous system subjective symptoms and signs (asthenia, memory and attention disturbances, irritability, vegetative disorders, headaches, dizziness, etc.). These findings seem to be more frequent in exposed and seems to be correlated with the exposure length.

Conclusions: Significant levels of EMF occupational exposure levels were found. Higher exposures are attributable to practice procedures, to peculiar electrotherapy procedures, to bad positioning of ETE, and to older generations of ETE. The lack of risk knowledge is an important factor for some exposure situations, but it could be corrected. Health findings point out to possible effects at higher levels but further studies should be done. Risk awareness policies are to be performed for both employees and decision factors.

Analysis of electric network data in the EXPERS study

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Abstract

The Health Ministry initiated a study on the personal exposure of the French population to 50 Hz magnetic field. One of the points of interest of this study is the contribution of each exposure source to the total exposure. We focus here on electric networks. The different data of the study, which includes a little more than 2000 subjects, allow us to identify for some subjects the presence of one or several networks close to home. The distance for taking such networks into account depends on the type of network: we considered all distribution and transport networks, as well as electric train networks. From magnetic fields measurements, after we checked whether the identified networks are really influencing the exposure of subjects. The results depend on the type of network.

Introduction

The French Ministry of Health initiated a study on the personal exposure to 50 Hz magnetic field of the French population (Souques et al. 2008). The global results of this study, called EXPERS, are presented in another communication (Bedja et al. 2010). A point of interest is the contribution of each source of exposure to the total exposure. We focus here on electric networks.

Material and methods

MV2, poll institute in charge of the collection of data, collected for each subject:

- 24h magnetic field measurement
- timetable
- general questionnaire about home and electric appliances used
- GPS coordinates of the home
- Address of the home

For each type of electric network (low to very high voltage), we determined the maximum distance at which the magnetic field generated by the electric network remains theoretically measurable in a residence. This distance was calculated for overhead power lines of voltage 63kV and higher by simulating magnetic fields generated by the different types of networks, in the middle of the span and with the annual mean current. The distance kept is the one where the mean calculated magnetic field is less than 0.1 µT. The magnetic field depends also on the geometry of the line and the distance kept was the largest of the distances calculated for different geometries.

Note that for train networks, a distance of 200 m was arbitrarily chosen. The transport like metro or tramway were not taken into account.

All subjects within these corridors were arbitrarily classified as "exposed" to magnetic fields generated by electric networks. The address of the home was converted into Lambert II étendu coordinates (French Lambert coordinates) by RTE (the French electricity transport network operator). The results of this calculation was validated by comparison to GPS coordinates measured.

The "exposed" subjects were identified from the addresses of subjects of EXPERS study by the network operators using their geographical data bases (all data not yet available for ERDF (the French electricity distribution network operator), the low and medium grid operator in France).

However, as the width of the corridor is overestimated, it is important to know, for the subjects arbitrary classified "exposed", whether their magnetic field measurements show or not the influence of electric networks. Indeed, the variation over one day of the field generated by electric networks is quite characteristic, and a visual check generally allows to confirm or not the contribution of one (or several) electric lines to the magnetic field record.

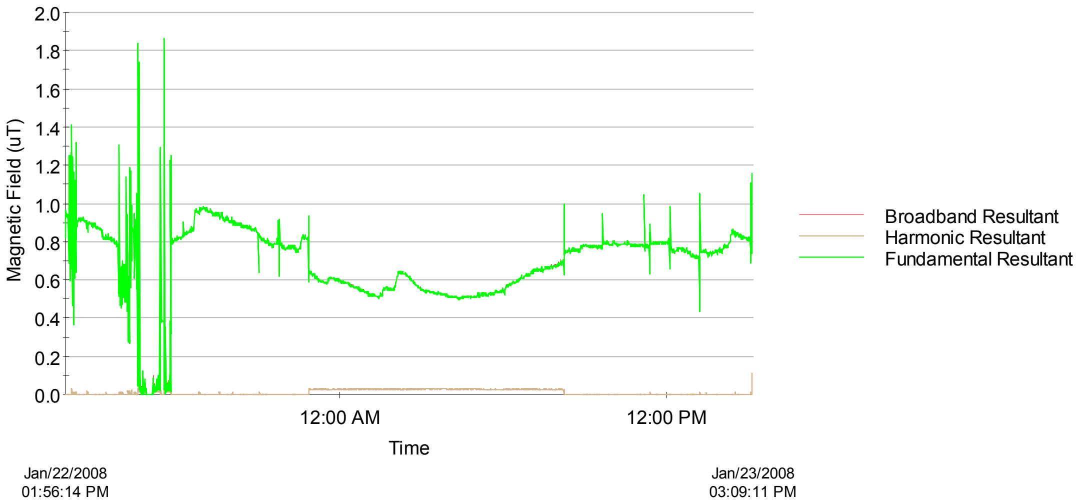

Figure 1. example of a subject really exposed to the magnetic field generated by a high voltage power line.

Figure 1 gives the example of a subject where the source is a high voltage overhead power line. The characteristics are a signal with little noise and proportional to a load curve of a power line, i.e. maximum at the end of the day, decreasing during the night then increasing again in the morning.

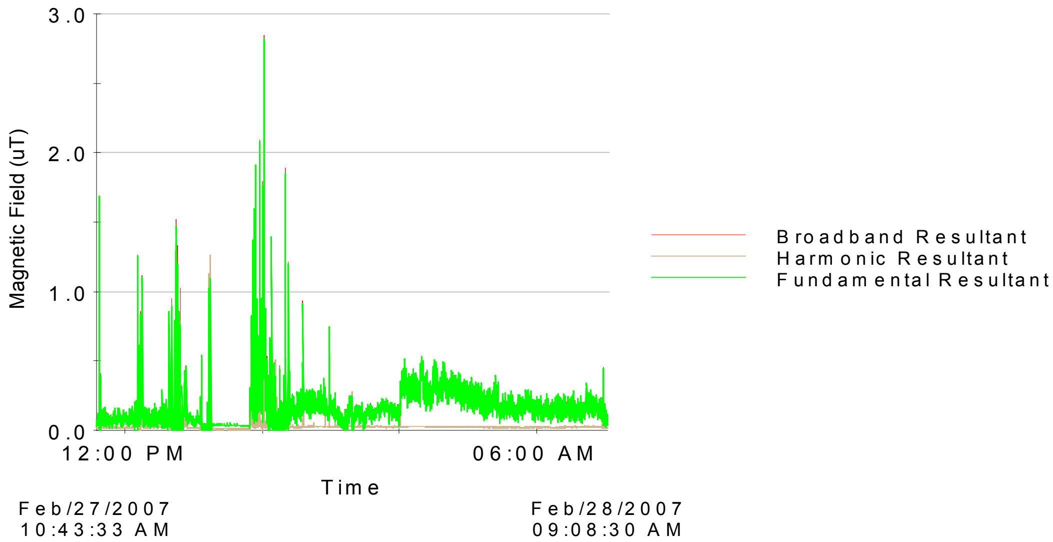

Figure 2. example of a subject really exposed to the magnetic field generated by a middle voltage power line.

Figure 2 gives an example representative of a subject where the source could be a middle voltage underground network. The signal presents the trend of a load curve during the night, but is noisy.

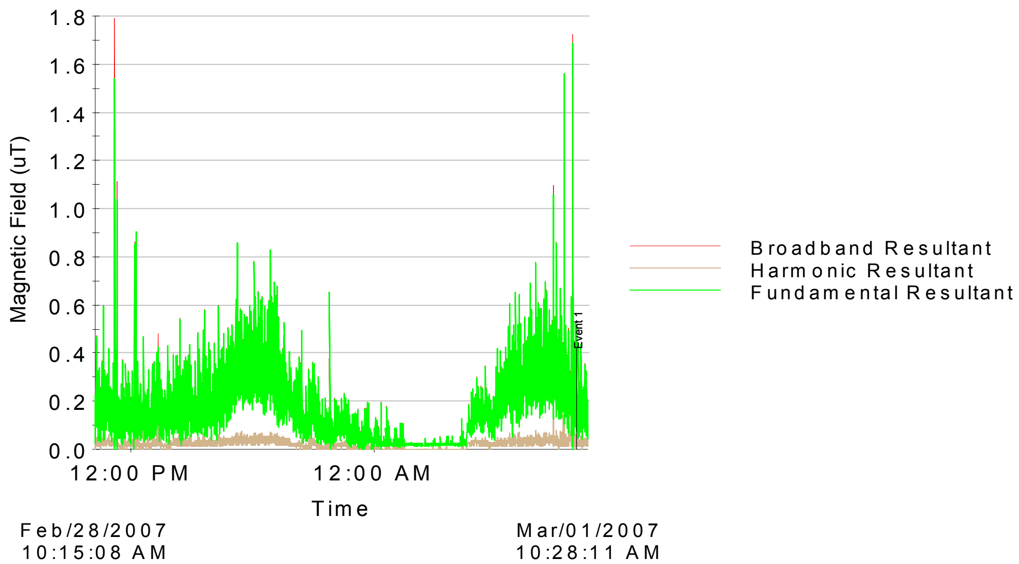

Figure 3. example of a subject really exposed to the magnetic field generated by a train line.

Figure 3 gives the example of a subject where the source is a train line. The characteristics are: a very noisy signal, proportional to traffic (maximum the evening and the morning, zero during the night), and with a ratio of harmonics above zero.

Signals are obviously not all as clear as in the examples given above. A lot are barely detectable and at the limit of ground noise. In order to privilege a conservative approach, we noted as “really exposed” all subjects as soon as we noted a very low tendency at the limit of ground noise.

Results

The EXPERS magnetic field database contains 2048 volunteers and 1581 addresses. There are less addresses than subjects because an adult and a child of the same family could participate in the study.

Table 1 gives the corridor width taken into account around electric networks, in function of the type of networks.

The position of RTE and ERDF networks is known with a precision of 10 m. For electric train networks, a distance of 200 m was chosen because of a lower precision on the position of networks, determined from IGN[1] data, with a precision around 100 m.

Table 1. Definition of corridors around electric networks.

Type of network	Distance (m)
400 kV overhead line	200
225 kV overhead line	120
150 kV overhead line	100
63 and 90 kV overhead line	70
Low voltage to 20 kV overhead line	20
Train line	200
Underground line 225 kV	20
Underground line 63 to 150 kV	20
Underground line low voltage to 20 kV	20
MV/LV substation	20

The number of « exposed » subjects varies between 9 for 400 kV lines (table 2), 162 for train lines (table 3) to more than 1024 for low voltage underground lines (table 4).

Table 2. Distribution of subjects « exposed » to magnetic field generated by RTE networks (data February 2010).

	Number of addresses	Number of individuals	remarks
Overhead line 400 kV	7	9	6 addresses (8 individuals) « exposed » to several lines
Overhead line 225 kV	9	13	
Overhead line 63 to 150 kV	20	26	
Total Overhead line	35	46	
Underground line 225 kV	16	17	5 addresses « exposed » to several lines
Underground line 63 to 150 kV	18	20	
Total Underground line	34	37	

[1] Institut Geographique National

Table 3. Distribution of subjects « exposed » to magnetic field generated by train lines.

	Number of addresses	Number of individuals	remarks
Train line	128	162	70 individuals are in Ile-de-France - 2 individuals with TGV line

Table 4. Distribution of subjects « exposed » to magnetic field generated by ERDF networks (data available today for 1565 individuals over 2032).

	Number of addresses	Number of individuals	remarks
Overhead line 20 kV	25	35	Provisional figures
Overhead low voltage line		620	
Total Overhead line		639	
Underground line 20 kV	455	543	
Underground low voltage line		880	
Total Underground line		1024	
MV/LV substation	60	66	
From which MV/LV substation in building	23	23	

Table 5. Analysis of the magnetic field measurements for subjects « exposed » to magnetic field generated by electric networks.

	Number of individuals	Measurements with influence of an electric network	Remarks
Overhead line 400 kV	9	7	
Overhead line 225 kV	13	11	
Overhead line 63 to 150 kV	26	8	
Underground line 225 kV	17	6	
Underground line 63 to 150 kV	20	8	
Train line	162	37	2/3 in Ile-de-France
Overhead line 20 kV	35	2	Provisional figures (analysis ongoing)
Low voltage overhead line	620	At least 54	
Underground line 20 kV	543	116	
Low voltage underground line	880	At least 115	
MV/LV substation	66	12	
Fro which MV/LV substation in building	23	4	

The visual analysis of measurements for all "exposed" subjects (table 5) shows that the magnetic field generated by the networks was detected in a proportion varying from 85 % of subjects "exposed" to magnetic field generated by very high voltage overhead power lines to 20 % of subjects exposed to magnetic field generated by train lines and less than 10 % of subjects "exposed" to magnetic field generated by 20kV overhead lines.

Discussion

This result must however be balanced by the following remark: the magnetic field measured is the result of the summation of magnetic fields emitted by all magnetic field sources, and not only by electric networks detailed here. As such the results are quite reliable for high voltage overhead lines and train lines whose signals are well characterised on the measurements, but for underground networks, substations and low voltage lines, the signal is at the limit of ground noise and non specific.

For example, for the individuals noted "exposed" to a magnetic field generated by MV/LV substation in buildings, and whose measurements are reflecting an electric network, no one is living at immediate proximity of a substation: the magnetic field "seen" on the measurement is thus not due to the substation.

In the same way, a part of the individuals noted « exposed » to a magnetic field generated by an underground line are living in buildings on a floor too high for underground networks be able to influence their exposure: it could be in this case the electric networks of riser shafts in buildings. A more detailed analysis will be necessary on this point.

Conclusions

This paper shows that:

– the part of the population whose exposure to 50 Hz magnetic field is influenced by high voltage power lines is small,
– the criteria of distance chosen in this study is maximizing and thus overestimates logically the number of people whose exposure to 50 Hz magnetic field is influenced by electric networks,
– it is not conclusive that underground electric networks are really the source of exposure seen in some measurements.

This study will continue with the analysis of all ERDF network data.

To discriminate the real influence of underground networks, it should be necessary to:

– look at the influence of the parameter "floor of the building",
– look at the measurements of individuals noted as "non exposed" to magnetic field emitted by an electric network, to see whether all are presenting exposures non influenced by electric networks or whether if some are presenting exposures influenced by electric networks, which would accredit the hypothesis of the influence of electric networks from riser shafts in buildings.

Acknowledgment

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On implementation of the new methodologies concerning measurement of occupational electromagnetic field levels

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Abstract

Measurement of electromagnetic field levels is a very important step in assessing human exposure to electromagnetic fields present in the working environment. After the year 2000, the methodologies on electromagnetic field measurement have been much developed and improved and, at present, there is a big number of technical standards dedicated to various exposure situations.

The implementation of the new methodology on electromagnetic field measurement in the national practice might be difficult, expensive, time consuming and it requires high qualified and special trained personnel. Considering the big change in the methodology to be applied, we analyze the limitations, difficulties and errors that might alter the quality of field measurement and exposure assessment.

To overcome the temporary lack regarding the good knowledge and clear understanding of the new methods, the authors propose a simple strategy consisting in a few steps. A general methodology was elaborated to be assimilated by the personnel involved in this domain, before learning complex methods. Standardized models of measurement report have been proposed. To ensure a solid background, training activities of measurement operators should be carried out by experts.

In agreement with European demands, some specific measures have been proposed to be taken concerning information dissemination, consultancy activities and, if the case, classification of measurement service providers into basic level and high level services. As an example, our activities in Romania in this domain are briefly described.

Microlens formation as protective mechanism against direct laser radiation

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Abstract

Laser radiation poses a significant threat to human eyes. Depending on power, even scattered radiation can produce damage (mostly to retina), not to speak of direct laser beam. The usual method of protection is through different kinds of filters (absorption, reflection, polarization, holographic) inside goggles or protective windows. Without exception all types of filters protect human eye from scattered or otherwise diffuse reflected laser light. All manufacturers of laser goggles specify that the eye is not protected against direct laser beam. We describe a novel principle of eye protection which is based on expanding laser beam by the filter material itself. In other words, when the laser beam hits the filter material, negative (diverging) microlens is formed almost immediately. The beam is strongly expanded by the microlens, thus reducing the energy density to tolerable level. To test the idea we have developed a suitable material – tothema sensitized gelatin. Tothema is a trade-name of a mixture of gluconates used to treat anemia. Mixture is added to ordinary cooking gelatin, rendering the material sensitive to laser radiation. Sensitivity was further enhanced at 532 nm by additionally doping material with eosin or betanin. Experiments have shown that upon irradiation, strong microlens (focal lengths far below -1 mm) forms quickly and the laser beam diverges, reducing the overall energy density. Results of measurements of dynamics of the process are shown.

Biological hazard of low-intensity radio frequency electromagnetic fields – Model experiments with protozoa

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Abstract
The effects of low-intensity 1 GHz (a mobile connection frequency) and 10 GHz (radar and satellite communications) electromagnetic radiation with energy flux density (EFD) of 5, 10 and 50 μW/cm^2 on a laboratory population of unicellular aquatic organisms – ciliates *Spirostomum ambiguum* were studied. The effects were registered by the criterion of change in spontaneous motor activity (SMA). SMA of ciliater was observed under the microscope. Two lines were deposited in the eyepiece of the microscope, crossing each other at right angles. A quantitative measure of motor activity of each ciliate was a number of intersections of the lines on the eyepiece of the microscope for 1 min. To do this, each ciliate was placed individually in a drop of water in a special cell with holes 5 mm in diameter and 2 mm in depth.

Sp.ambiguum used for a long time to estimate the negative effect of chemical and physical factors on the environment. These ciliates have proved to be a sensitive bioindicator of low-intensity influences. Our research has shown that electromagnetic radiation reduces motor activity of ciliates already at such low levels of exposure as 10, 45 minutes and 8–9 hours respectively with EFD 50, 10 and 5 μW/sm^2. The negative effect did not depend on a frequency of electromagnetic radiation in the diapason from 1 to 10 GHz. The effect had a threshold character. After reaching the threshold, the negative effect did not change with exposure and had a mass character. The level of SMA in the population of ciliates decreased at 40%. The negative effect transmitted to descendants of irradiated ciliates. The results were confirmed by independent experiments involving more than 5000 *Spirostomum*.

Our results are interesting for practical using of protozoa's behavioral reactions for testing of biological hazard of electromagnetic pollution of aquatic environments. It is of interest as the general problem of electromagnetic activity on the biota.

Introduction
It is known that not only sufficiently powerful fluxes of energy (in tenths of W/cm^2) of radio frequency electromagnetic fields (EMF) have had a negative impact on organisms. The negative biological effect occurs when the energy flux density (EFD) is comparable with the level in tens and units of μW/cm^2. Such levels of EFD are

observed in many workplaces and places of human habitation. Interest in the biological effects of low intensity electromagnetic fields has increased significantly with the advent of mobile communications.

Experts did not have general opinion about safety of radio frequency electromagnetic radiation with nonthermal power in spite of the duration studies with help of different biological subjects. There are opposing points of view. This is reflected in huge differences of the maximum allowable levels (MAL) of electromagnetic fields which are recommended in different countries. Until recently, differences in the MAL for the population in different countries were to 1000 times. In Russia the MAL installed as 10 μW/cm^2 (Sanitary rules and norms 2.1.8/2.2.4.1190-03, Russia), that is less than in Europe and in the USA. These regulations, however, are not sufficiently substantiated. The experimental data are contradictory. The theoretical justification is absent.

The biological risk of electromagnetic radiation has been studied with help of very labor-intensive methods. It hampered the expansion of research. We used an express method which is based on a quantitative assessment of changes in spontaneous motor activity of aquatic ciliates *Spirostomum ambiguum* Ehrbg (Tushmalova et al 1998). The toxicity of pesticides, heavy metals, phenols and other factors, including those at low doses of agents, as well as the differentiation of spirostomum's motor activity by alpha- and beta-irradiation were detected within 1-2 h (Tushmalova et al 1998; Tseplin et al 2005; Sarapultseva 2008). High sensitivity of this method was shown in all cited works. We carried out several studies of the influences of radio frequency electromagnetic fields on the motor activity of *Sp.ambiguum* (Sarapultseva et al 2008; Sarapultseva et al 2009). The results, in our opinion, have the theoretical and practical interest. We found negative effects of low-intensity 1 GHz (a mobile connection frequency) and 10 GHz (a frequency of radars, satellite television, radio, wireless computer networks, satellite navigation, etc) electromagnetic radiation. The negative effects of electromagnetic radiation i) was manifested at low energy flux density, ii) did not change with increasing exposure of EMF in a wide time range, and iii) was inherited during vegetative reproduction.

Let’s consider the obtained results.

Material and methods

Ciliates were cultured at 20 ± 2^{0}C in the biological test tubes with tap water, devoid of chlorine. Installations for the electromagnetic irradiation of biological samples consisted of generators, antennas and cables which were giving energy in the mode of continuous generation. The energy flux density had regulated in accordance to the established relationship for each frequency electromagnetic radiation.

Ciliates were irradiated in the mass culture in Petri’s plastic dishes with a diameter of 4 cm and 0.3 cm layer of water. The time of exposure in the electromagnetic field was dependent on the energy flux density and ranged from 5 minutes to 16 hours. The control groups of ciliates were in similar conditions, but without the influence of electromagnetic fields.

Quantify changes in motor activity of ciliates was carried out immediately after irradiation. To do this, 20 ciliates were selected randomly from mass culture, which was irradiated with the frequency of 1 or 10 GHz and energy flux density of 5 or 10 or 50 μW/cm^2 and during from 5 min to 16 h. Spontaneous motor activity (SMA) of ciliates from the control groups was tested at the same time. Ciliates from irradiated and control groups were placed individually in a drop of water in special plastic plate with holes of 5 mm in diameter and 1-2 mm in depth. SMA of each ciliate was observed under the microscope. At the eyepiece of the microscope were did two lines crossing each other perpendicularly. A quantitative measure of motor activity of each ciliate was the number of intersections of the lines for 1 min.

The ciliates after irradiation were continued to cultivate at optimal condition in order to clarify the question of inheritance of negative effects of low irradiation. The effect of irradiation was estimated by reduce of motor activity in the experimental groups of ciliates. These changes were measured immediately just after irradiation and at the 4th, 14th, 21st and 30th days.

It was held on 3–5 series of observations at each case. Thus, it was tested more then 5 000 ciliates. Assessing the reliability of experimental data was carried out with help of the nonparametric Fisher test.

Results

Study of biological electromagnetic radiation effects at 1 GHz with a flux density of energy 10 μW/cm^2

First, consider the results of low-intensity electromagnetic radiation at a frequency of mobile communications (1 GHz) with the maximum allowable in Russia energy flux density 10 μW/cm^2. The change in ciliates' motor activity after radiofrequency exposure duration 15–60 minutes you can see in the Table 1.

Table 1. Changing in ciliates' motor activity (in absolute terms and in % relative to control) just after radiofrequency exposure duration 0.25-1 h at 1 GHz (EFD 10 μW/cm^2).

The exposure time, minutes	$M \pm m$	%, $(M_{exp}/M_c)\cdot 100$
0 (Control)	2.15 ± 0.18	100.0 ± 8.4
15	2.20 ± 0.17	102.3 ± 7.7
30	1.80 ± 0.21	83.7 ± 11.6
45	1.20 ± 0.15*	55,8 ± 12.5*
1	1.25 ± 0.17*	58.1 ± 13.6*

* $p \leq 0.05$
M±m **– average motor activity with a standard error**
***M_{exp}* – motor activity in experiment**
***M_c* – motor activity in control**

Statistically significant ($p \leq 0.05$) decrease in motor activity of ciliates occurs "abruptly" after 45 minutes stay in the EMF at 1 GHz and EFD 10 μW/cm^2. Table 2 presents the results of observations in 3 series of experiments at the threshold exposure time of 45 minutes.

From Table 2 shows that the average SMA of ciliates in the experimental groups is significantly lower than SMA in the controls groups. Change in motor activity is well reproduced in all series of experiments and differs by 40–45% of control.

In subsequent experiments the effect was studied with increasing exposure in EMF. At Figure 1 shows the results of change in motor activity of ciliates immediately after RF exposure in a wide time interval from 15 minutes to 10 hours.

Table 2. Changing in ciliates' motor activity in control and after exposure at 1 GHz during 45 minutes in three series of experiments.

№ Experiments	Control, $M_c \pm m_c$	Experiment, $M_{exp} \pm m_{exp}$	%, $(M_{exp}/M_c) \cdot 100$
1	2.10 ± 0.18	1.20 ± 0.15*	57.1 ± 12.5*
2	2.25 ± 0.18	1.32 ± 0.17*	59.2 ± 13.0*
3	2.20 ± 0.15	1.15 ± 0.19*	52.3 ± 16.5*
Average	2.18 ± 0.16	1.22 ± 0.17	55.9 ± 13.9

*** $p \le 0.05$**
***$M \pm m$* – average motor activity with a standard error**
***M_{exp}* – motor activity in experiment**
***M_c* – motor activity in control**

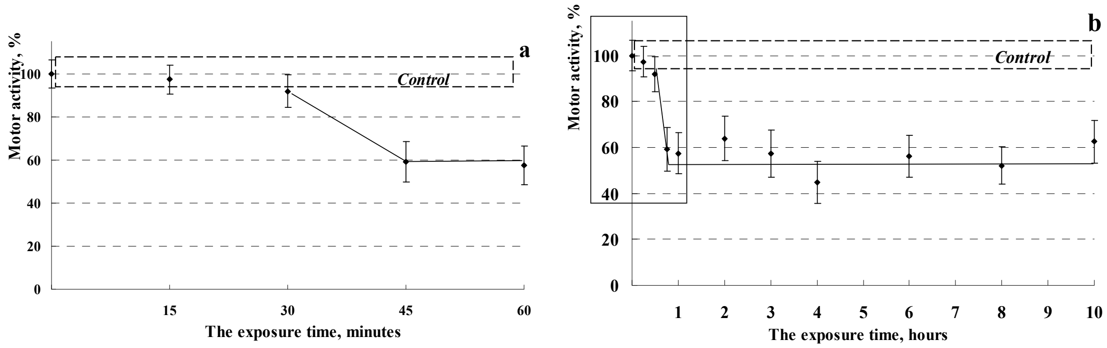

Fig.1. Changing in ciliates' motor activity (in% relative to control) at the electromagnetic irradiation with 1 GHz and 10 μW/cm^2 duration up to 60 minutes (a) and up to 10 hours (b).

The differences in ciliates' motor activity between the experimental groups and controls are evident, equal and don't change with increasing exposure from 0.75 to 10 h.

Study of biological electromagnetic radiation effects at 10 GHz with a flux density of energy 10 μW/cm^2

At Table 3 shows the changes in motor activity of ciliates immediately after exposure of up to 10 hours at a frequency of 10 GHz.

Statistically significant ($p \le 0.05$) decrease in motor activity occurs "abruptly" after 45 minutes stay in the EMF. That time coincides with the time of the "safe" location in the EMF with the parameters of mobile communication (Table 1 and 2). Table 3 also shows that the negative effect produced by radiofrequency exposure within 45 minutes, didn't change even with increasing exposure time to 10 hours.

Save a negative effect in the generations of ciliates

Let's consider the results of motor activity's changes in the offspring of irradiated ciliates. Figure 2 shows the change in motor activity of ciliates on the 4^{th} (a), 14^{th} (b), 21^{st} (a) and 30^{th} (d) days after exposure.

Table 3. Changes in ciliates' motor activity (in absolute terms and in% relative to control) immediately after radiofrequency exposure duration of 0.25–10 h at 10 GHz (EFD 10 μW/cm^2).

The exposure time, h	$M \pm m$	%, $(M_{exp}/M_c)\cdot 100$
0 (Control)	2.14 ± 0.06	100.0 ± 2.8
0.25	2.09± 0.10	97.7 ± 4.8
0.50	1.95 ± 0.09	91.1 ± 4.6
0.75	1.33 ± 0.08*	62.2 ± 6.0*
1	1.24 ± 0.06*	57.9 ± 4.8*
2	1.19 ± 0.10*	55.6 ± 8.4*
3	1.13 ± 0.07*	52.8 ± 6.2*
4	1.08 ± 0.06*	50.5 ± 5.6*
6	1.34 ± 0.08*	62.6 ± 5.9*
8	1.42 ± 0.12*	66.4 ± 8.5*
10	1.42 ± 0.09*	66.4 ± 6.3*

*** $p \leq 0.05$**

$M \pm m$ – Average motor activity with a standard error
M_{exp}* – *motor activity in experiment
M_c* – *motor activity in control

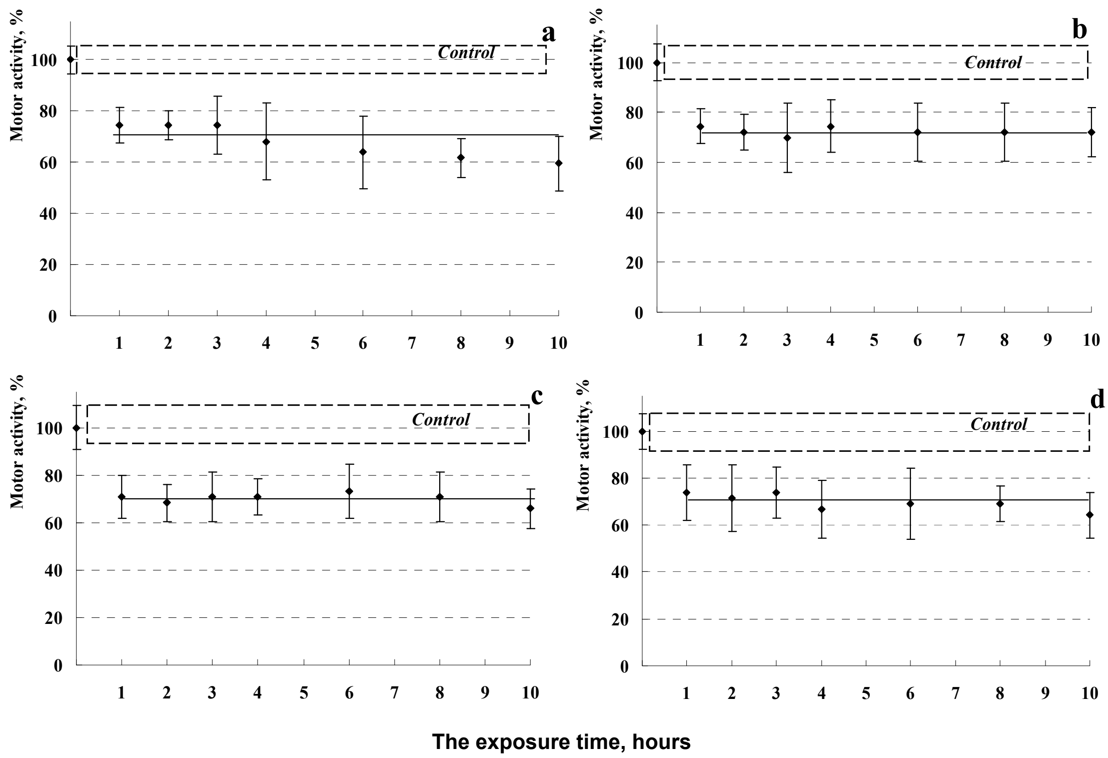

Fig. 2. Changes in ciliates' motor activity (in% relative to control) after radio frequency exposure at 10 GHz and 10 μW/cm^2 on the 4^{th} (a), 14^{th} (b), 21^{st} (c) and 30^{th} (d) days

Figure 1 shows that the significant decrease ($p<0.05$) in SMA was approximately the same at all times (immediately and in distant periods after exposure) and at all period of irradiation. That effect took place at exposure from 1 to 10 h. The effect was recorded on the 30th days after irradiation. During that time the ciliates replaced about 10–12 generations (average length of the cell cycle was about 2 days (Wichterman R., 1953). It follows that the effect can transmitted to descendants of irradiated cells.

Study of biological hazards of electromagnetic radiation at different radio frequency energy flux density

Figure 3 shows the results of changes in motor activity of ciliates at electromagnetic radiation at a frequency of mobile communications (1 GHz) with EFD 5 μW/cm^2.

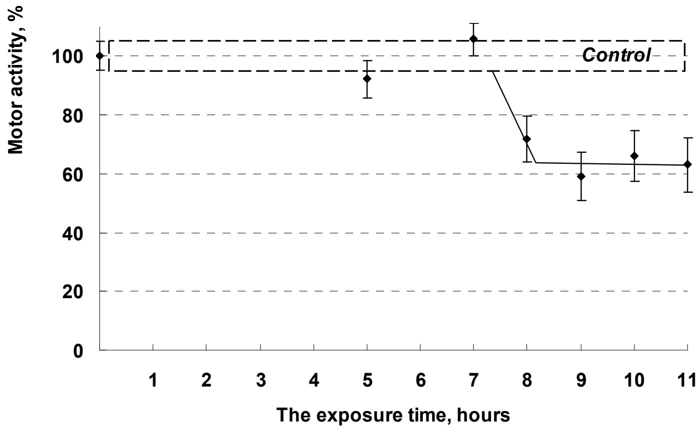

Fig. 3. Changing of ciliates' motor activity in electromagnetic field with EFD 5 μW/cm^2 at 1 GHz up to 11 hours.

Recall that such energy flux density is in 2 times less than the maximum allowable level in Russia. However, Figure 3 shows that the ciliates' motor activity reduces about the same as it is in the electromagnetic field with the energy flux density of 10 μW/cm^2. Decreased of motor activity occurs, however, after much longer exposure, after 8–9 h. The effect in that case when the exposure reached a threshold no longer depends on the duration of exposure. The saltatory nature of the effect in these experiments was clearly registrated. If a 7-hour exposure was not causing reduction of spontaneous motor activity, the 8-hour exposure caused this effect. Increased exposure time up to 9, 10 and 11 h hadn't influence on the degree of change in ciliates' motor activity. The time which ciliates spent in the electromagnetic field with a lower energy flux density of 5 μW/cm^2 (when the changes in ciliates' motor activity did not occur) increased in 16 times (from 45 min to 8-9 h) compared with the exposure time in the EMF with the energy flux density of 10 μW/cm^2.

The overall pattern and degree of changes in SMA were the same after irradiation at a frequency of 1 GHz with an even higher energy flux density – 50 μW/cm^2. The effect was absent in a certain time range, but then the motor activity of the experimental ciliates abruptly decreased by about 35–40%, as happened in previous cases. In the case when the energy flux density was 50 μW/cm^2, irregularities in the motion ciliates occurred with exposure of no more than 10 minutes.

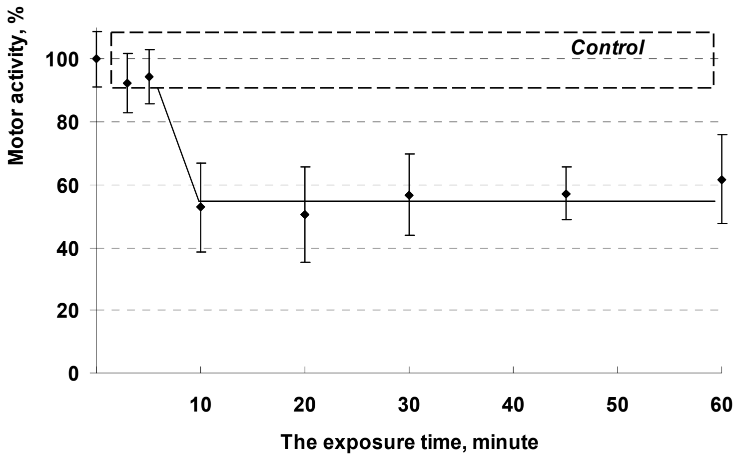

Fig. 4. Changing of ciliates' motor activity in electromagnetic field with EFD 50 μW/cm^2 at 1 GHz with exposure of 1 minutes up to 1 hours.

Next, we evaluated the biological effectiveness of EMF at a frequency of 10 GHz. The degree of inhibition of ciliates' motor activity was significant and approximately equal and didn't changed with increase of energy flux density from 5 up to 50 μW/sm^2. However, the time of occurrence of dysfunction movement depended on the energy flux density. The safe duration of exposure at 10 GHz was about 8–9 h, 45 and 10 minutes respectively with the EFD of 5, 10 and 50 μW/cm^2 as was observed at a frequency of 1 GHz (figure 5).

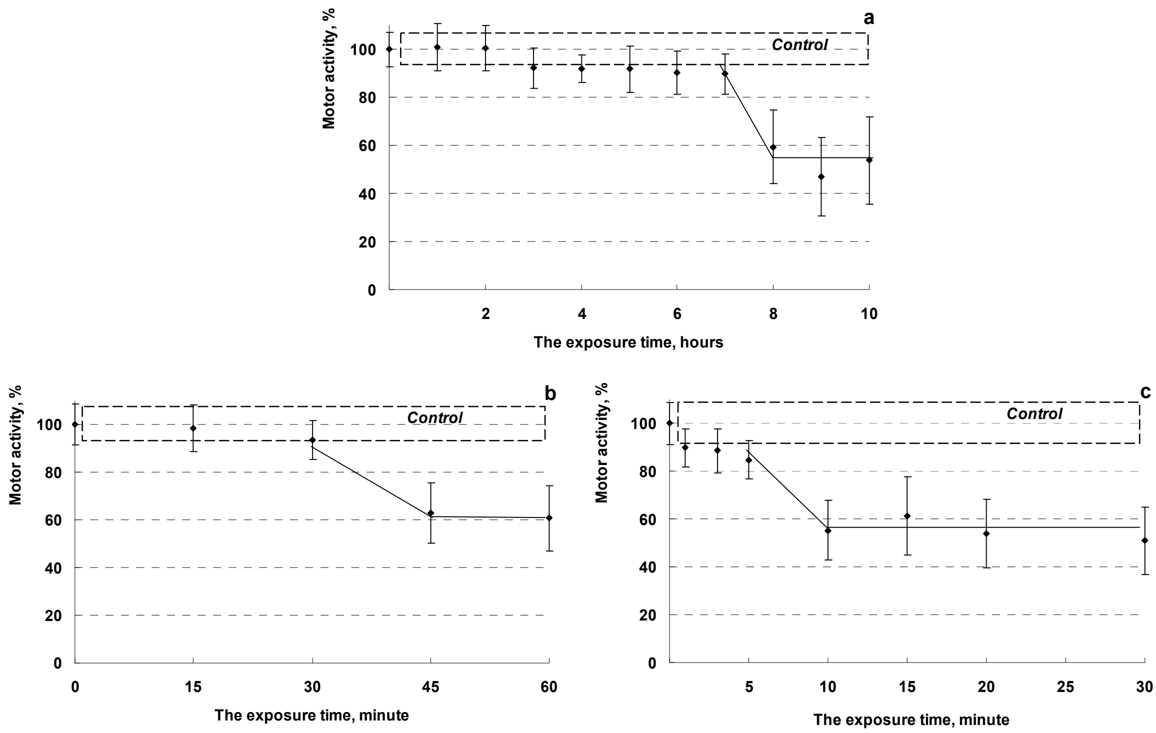

Fig. 5. Changing of ciliates' motor activity in electromagnetic field at 10 GHz with EFD 5 (a), 10 (b) and 50 (c) μW/cm^2.

From Figure 5 shows that the extent and nature of the effect of electromagnetic radiation at a frequency of 10 GHz was not appreciably different from those which were found after irradiation at the frequency of mobile communications 1 GHz (Fig.3 – 4 and Tabl.3). Decrease in ciliates' motor activity was approximately 40%. The degree of change in the ciliates motor activity wasn't depended of the time of exposure after reaching a threshold.

Discussion

The study shows that even very low levels of electromagnetic radiation of radio frequencies, which is widely used by people, could harm the function of motion of the representative biota. A massive inheritable independent from duration of electromagnetic irradiation a decrease of ciliates' motor activity is unusual phenomenon for low-intensity non-ionizing radiation.

However, the results are quite consistent with the data obtained by us after γ-irradiation *Sp.ambiguum* in a wide range of doses, including the low doses (Sarapultseva et al., 2008). A mass effect of decreasing the viability of individuals in populations of other species of ciliates (*Paramecium caudatum, Climacostomum virens*), amoebae and mammalian cells after exposure to low doses of radiation was described also in the book of I.Bychkovskaya et al (Bychkovskaya et al., 2006 http://irbb.ucoz.ru). These violations persisted in remote periods after irradiation – inherited. This proves the reality of the effect and assumes a possible common mechanism of biological action of low-dose of electromagnetic radiation of different nature.

The data about the occurrence of negative effect in motor activity of ciliates after relatively low electromagnetic effects in the early periods after irradiation and irreversible transfer to the progeny rule out the possibility of mutational nature of these changes. We assume that one possible mechanism is a change in the structure of DNA. It is the basis of epigenetic inheritance (Jablonka E. et al., 2008).

Despite numerous studies to date were not significantly determined the basic mechanisms (except thermal) effects of electromagnetic radiation on biological subjects. There are recent theoretical developments and some, though not indisputable facts that the electromagnetic radiation is not only a background against which the unfolding basic biological processes, but it plays a decisive role in all processes of exchange. Several studies show that water plays a decisive role in the effects of electromagnetic radiation on biota. The observed biological effects of low doses of electromagnetic radiation may be due to the formation of reactive oxygen species in the aquatic environment. This is accompanied by stronger oxidative process and the formation of a large number of free radicals that bind to protein components (especially in the tissues which involved in metabolism). It is known that free-radical processes violate the metabolism of DNA, causing mutations. It violates the complementarily of the structure of DNA, breaking hydrogen bonds; induce chromosomal and genomic disorders. Such processes are for non-thermal electromagnetic radiation. The specificity of the non-thermal radiofrequency electromagnetic field is determined of the resonance character of the energy and informational nature. The primary effect is realized at the cellular level and is associated with elements of cytoplasmic membrane, in particular, molecules of proteins and enzymes with a significant electric dipole moment.

Conclusions

We obtained the data that the negative effect of electromagnetic radiation to ciliates' motor activity takes place already at the maximum allowable, and even in two times lower than maximum allowable limit of energy flux density. It is shown that the nature and extent of damage from electromagnetic radiation with frequencies differing by ten times (1 and 10 GHz) are virtually identical. Those are of particular importance in terms of EMF practical application. This is interesting in connection with the problem of standardization of EMF on biota.

Analysis of the new data will be interesting as a fundamental aspect in the discussion of dose-independent reactions, which were obtained in different biological subjects after low radiation (Bychkovskaya et al., 2006 http://irbb.ucoz.ru; Sarapultseva et al., 2008; Sarapultseva, 2008; Sarapultseva et al, 2010). In this case, however, remains an open question how formed the equal response to exposure of low doses of different agents if those agents are very differ among themselves on transferred energy. This question requires further experimental studies.

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Sunbed-usage by 12–23 year old in Iceland 2004–2009

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Abstract

In Iceland, polls have been conducted every year since 2004 among 1800 randomly selected individuals aged 12-23 years inquiring whether they used sunbeds in the previous 12 months. The intention was to determine the level of sunbed use by the young and to monitor the effectiveness of a yearly information campaign on the possible consequences of such usage.

On average; approximately 20% of those between ages 12 and 15 said they used sunbeds as compared to 52% of those aged 16-19 years. For the whole group of 12-23 years old, 41% reported using sunbeds.

A statistically significant 20% reduction in the number of users took place for the whole group aged 12-23. However, the reduction was smaller and statistically insignificant for those aged 12-15.

Introduction

In Europe, young people below age of 18 have long been discouraged from using sunbeds by mandatory user instructions in sunbed saloons. The effectiveness of this discouragement is not well known since data on the usage by the youngest users is scarce. Published information on sunbed use normally only spans age groups 18 year and older.

Concerns over a rising incidence of melanoma in Iceland, especially among young women, led to the formation of a UV-task group in 2004 by the Icelandic Radiation Safety Authority, the Cancer Society, the Association of Dermatologists, the Directorate of Health and the Public Health Institute of Iceland. Advertisements from sunbed saloons aimed at children preparing for their confirmation ceremony at the age of 13 to 14, prompted the group to employ Capacent-Gallup, a professional polling agency to monitor the sunbed usage of young people with annual user-polls.

Advertisements, prepared by an advertising agency (ENNEMM) were published on the 10th of March 2004 in newspapers with an open letter to parents, signed by the directors of the above named health authorities, see Figure 1.

Fig. 1. Advertisement aimed at parents. A confirmation figure with an imprint of sunbed-goggles in its face. The text asks parents to consider the health consequences of cosmetic tanning.

The advertisements were followed up by interviews with health specialists in the news-media. In the following years, similar activities have been repeated. In Figure 2 is an example of an interactive Internet banner prepared in 2008 to grab the attention of the young. This effort had support from newspapers, radio and TV-stations and received much attention.

Fig. 2. An Internet banner aimed at youths with a title in slang-language followed by a simple message: "Young people should not use sunbeds". When the lever is moved the smiley goes through several stages of burning (three are shown).

Material and methods

Data on sunbed usage was collected by Capacent-Gallup in Reykjavik, using 1800 randomly selected individuals aged 12-23, each year in March to May. During the first years, individuals were contacted by telephone, but presently the majority is polled through the Internet.

In the first few years, answers were received from almost 70% of those selected but this number is down to almost 50% in the most recent polls. This is however not believed to skew the results because the reason for declining response is not believed to be linked to sunbed usage. The questions on sunbeds are among many others that are mostly relevant to product marketing and responses to all polls have been decreasing in recent years. For children younger than 18 years, permission from parents must be sought which probably reduces the response rate.

When averages are made over different groups (sex, age, living in or outside Reykjavik), they are corrected for differences in group response.

Results

Usage percentages are presented in Table 1. Those who are 12 to 15 years old have not finished their compulsory schooling and are grouped together. Most of those aged 16-19 are in high school / junior college (Icelandic: menntaskóli, Danish: gymnasium) and many of those aged 20-23 are university students.

Table 1. Percentages of different age groups that said they used sunbed the previous 12 months.

Year	12 -15 year	16-19 year	20-23 year	12-23 year +/- 95% CI
2004	25%	56%	61%	46% +/- 3%
2005	13%	49%	57%	38% +/- 3%
2006	19%	51%	55%	40% +/- 3%
2007	21%	52%	52%	40% +/- 3%
2008	20%	56%	55%	42% +/- 3%
2009	21%	47%	43%	37% +/- 3%
Averages	20%	52%	54%	41%

The young people were also asked how often they used sunbeds. As could be expected, the age group 12-15, reported less use compared to users 16 years and older. Among the former, who used sunbeds at least once, around 15% used them monthly or more often, while some 28% of users in age group 16-19 and 24% of those aged 20-23 did the same (averages for the whole period). A corresponding number for 16-75 years old in 2004-2007 is reported as 19% in another study [1].

Figure 3 shows how the number of sunbed users has decreased for the population of young people aged 12-23. The decrease is 20% from the year 2004 to 2009 and statistically significant.

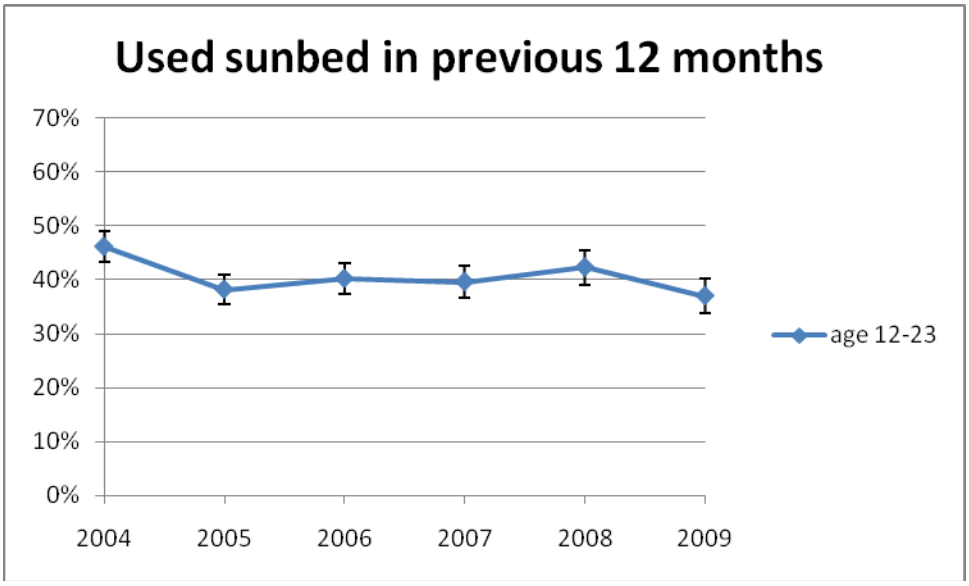

Fig. 3. Percentage of young people (age 12-23) that said they used sunbeds at least once the previous 12 months, both sexes and rural locations included. A 95% confidence interval is shown.

Figure 4 displays the change over time in sunbed usage for the three groups. The number of users 12-15 year old was almost halved the first year of active information dissemination, but it has grown since to similar level as it was earlier (the difference is statistically not significant). The number of sunbed users in age group 20-23 year old was however reduced by 30%.

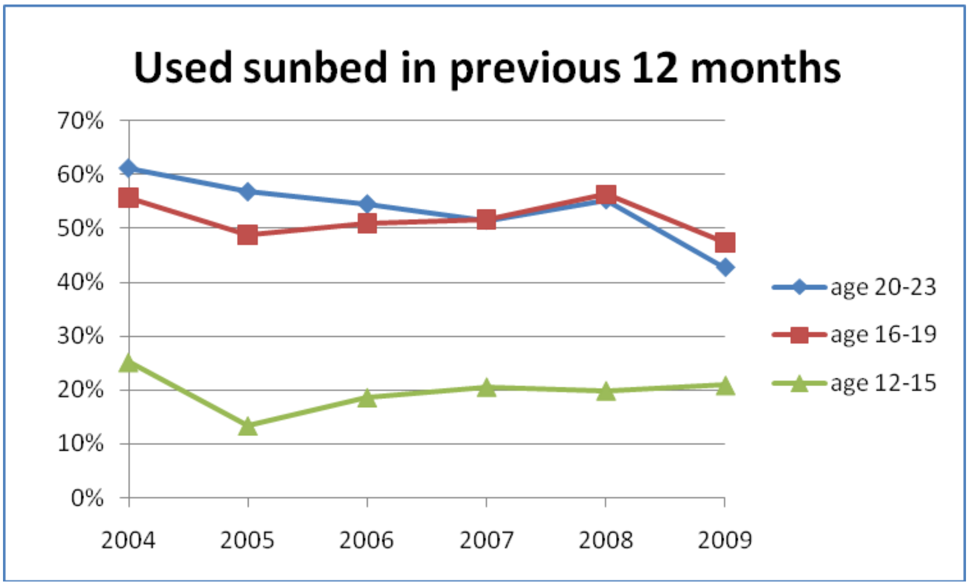

Fig. 4. Sunbed usage of three age groups. Confidence intervals are not shown but can be estimated to be ~√3 wider than in Figure 3.

Discussion

The results presented here are in line with data gathered by different means, see reference [1]. Information on sunbed numbers indicates that sunbed usage has been very common in Iceland but it has been reduced in recent years. It does not come as a surprise that sunbed usage was sharply reduced by children at confirmation age in 2004, it is more surprising how resilient this usage has later proven to be. The drop in sunbed usage reported in 2009 seems mostly to have affected adults and could be due to the sudden economic turmoil in Iceland in the late 2008.

The results seem to be internally consistent but there is no other data on the usage by 12-15 years old in Iceland with which to compare it.

In 2005 Nordic radiation protection authorities issued a common statement [2] strongly advising young people not to use sunbeds. The radiation protection agencies of Iceland, Norway, Finland and Sweden issued another statement 11th of November 2009 recommending regulation of tanning facilities that includes the prohibition of use for people below 18 year of age [3]. This recommendation was unanimously supported by the Icelandic UV-task group.

The government of Iceland decided in March 2010 to introduce a legislation to ban sunbed use by people less than 18 years of age. This legislation is now in preparation.

Conclusions

According to this study, 20% of 12 through 15 years old Icelanders used sunbeds in Iceland in 2004-2009. It has proven difficult to permanently decrease this usage through information campaigns. The campaigns have however been effective in reducing usage by adults who were not their primary target.

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Evaluation of low frequency magnetic field exposure system for ICDs for in vitro studies

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Abstract

This paper presents an in-vitro characterization set up of implantable cardiovertor defibrillator (ICD) immunity. A set up has been modeled by using a Helmholtz coil and an electric ad hoc interface. It generates and controls uniform magnetic fields. A comparison was made between the file that contains the parameters of emitted disturbances at a given time and the time of the occurrence of each event recorded by the ICD. This has allowed us to deduce the signal level that caused false detections in one case, or inhibition of the detection in the other case. Evidence is that the higher the level of disturbance, or when the frequency is in the "cardiac" frequency band, the number of false detections increases. One result is an amplitude "window effect" for the detection and dysfunction.

Introduction

Risks of electromagnetic fields (EMF) exposure associated with patients bearing medical implants such as the implantable cardiovertor defibrillator (ICD) are under a concern since this population is increasing. Cardiac devices are the most common medical implants(Nuegell et al 1996, Occhetta et al 1999) and are subject to specific international standards. However, since the European directive 2004-04 CE on the limitation of a worker's exposure to EMFs, supplementing the 1999/519/CE recommendation, many questions remain unanswered. Establishing a risk assessment procedure for workers with medical implants is very complex due to the diversity of potential situations involving EMF interactions in the professional environment. The effect of radio frequencies (RF) on ICD's has been widely investigated (Inrich et al 1996, Guertin et al 2007) and there are many papers in the literature describing the electromagnetic interference between ICDs and RF systems such as medical devices (X-rays), cellular phones and security systems (Inrich et al 1996, Mathew et al 1997, Shellock et al 2007).In addition, the effects of extremely low frequency (ELF) fields (e.g those generated by power lines for transport such as railways or for power supplying) have also been considered. The ICD bearer, until a few years ago, was typically excluded from his job after his implantation. Since ICD may concern also young people now, this situation implicates a real social problem when they come back to their work after surgery. Research has been performed on ICDs in the proximity of high voltage power lines (Souques et al 2002) and the susceptibility of implantable medical devices to the EMFs generated by electric security systems has also been investigated, highlighting transient anomalies (McIvor et al 1995, Mugico et al 2000). Nowadays, the average age of ICD bearers is decreasing, therefore, an ICD bearer could be working in a factory where high power machines generate EMFs. For example, in the proximity of high power welder machines (75 kVA), the magnetic field ranges from 100 µT (at 1.5 m) to 2000 µT (at 0.15 m) (Cooper et al 2002, Fetter et al 1996). In this sense, particular effort is devoted to analyze the electromagnetic interference (EMI) effects of ELF fields on cardiac implants, both from an experimental (Della Chiarra 2006) as well as from a theoretical simulation approach (Dawson et al 2002) .The exposure to uniform electric field and contact currents has also been investigated(Dawson et al 2000). Assessment of human exposure at the workplace for persons bearing active implantable medical devices in electromagnetic fields is thus a current challenge for all the concerned electrical industries. Previous relevant studies have already been conducted on pacemakers in vitro at the Laboratory of Electronic Instrumentation of Nancy (Nancy University) for frequencies of 50/60 Hz, (Scmitt et al 2005). In this paper we describe a method for the in vitro characterization of the immunity of ICD to electromagnetic interferences at low frequencies (50 Hz-60Hz).

Methods and materials

An experimental set up (Katrib et al 2009) using a source for environmentally relevant interferences consists of a programmable low frequency generator connected to a power amplifier then to a transformer to deliver a sinusoidal current connected to Helmholtz coils (uniform magnetic fields) to simulate the EMF. Helmholz coils and the device under test (DUT) are placed in a Faraday cage (fig 1).

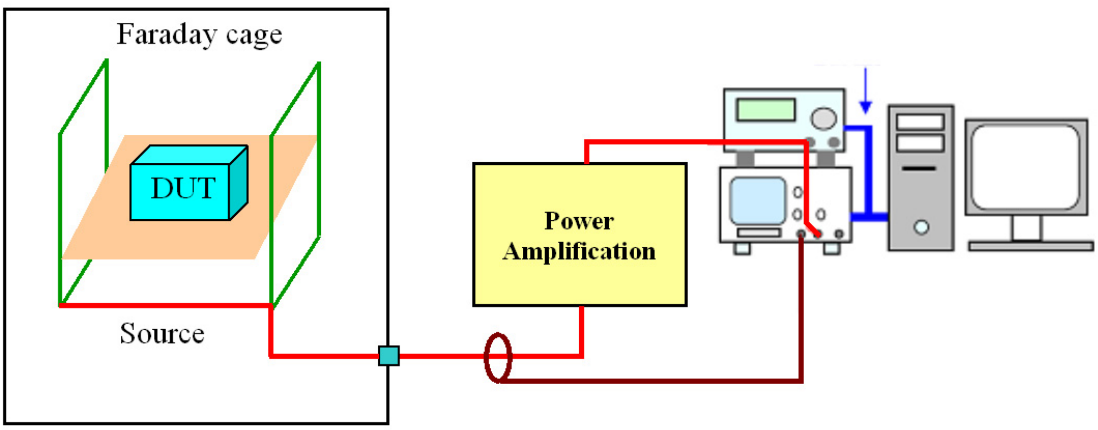

Figure 1 Experimental set up for testing the ICD immunity.

The entire set up is controlled with a PC by an IEEE488 connection and a data acquisition program that can control and communicate with a piece of test equipment to adjust the amplitude levels and frequencies of the EMF. The acquisition of these parameters is synchronized with the clock of the DUT, by a telemetric controller. The oscilloscope allows the monitoring of the signals during routine settings. The exposure system presented here offers the possibility to investigate the immunity of ICD to magnetic fields by placing the device, together with its leads, inside a homogeneous testing field. A Plexiglas support, holding the ICD and the leads in a well-defined position, is placed between the induction coils so that the DUT is positioned in the homogenous field volume for tests. This support may be used in the air as well as in a Plexiglas tank that can be filled with saline solution or gelatin mimicking electrical properties biological tissues (Marchal et al 1989). In latest study Silny (Scholten et al 2001) estimated the closed loop formed by the metallic housing and the tissues to 225 cm ^{2}, in unipolar detection. In this case big phantom was needed (45*30*24.5 cm) to simulate a realistic situation. In the bipolar detection we don't have this problem as the distance between proximal and distal electrodes does not exceed 2 cm. Our proposed tank simulator has a height of 12 cm and a length of 28 cm. Finally, the induction coils are placed on a wooden support to avoid distortion of the magnetic field.

Results

Figure 2 presents the electrocardiogram (ECG) registered when testing the ICD with a lure heart signal simulating a ventricular fibrillation. In this study, we apply an arrhythmic signal (fibrillation or tachycardia) during 15s followed by a normal rythme signal during 45s, so that the ICD is able to recover between each arrhythmic episode.

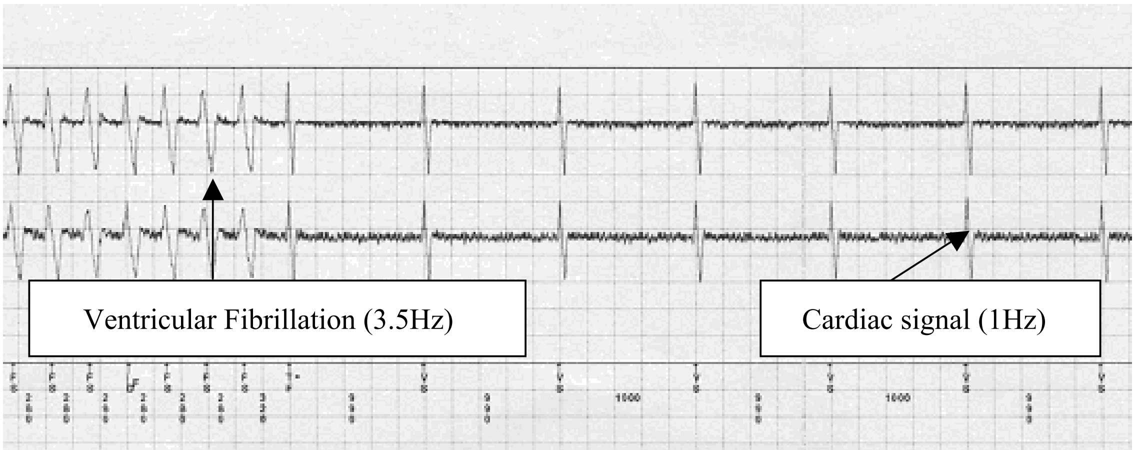

Figure 2 Chart of ECG during a simulated fibrillation episode.

Once the physiological signals are set up, we study the behaviour of ICDs in the VVI mode in order to plot the immunity of ICD versus applied magnetic fields. For magnetic fields up to 1000 μT, which is 2 times higher than the standard threshold for occupational exposure to magnetic fields, no interaction was found. Above 1000 μT, figure 3 and 4 presents the behaviour of ICD exposed to different inclinations angles of the magnetic field with respect to perpendicular exposure. One can remark that when the inclination angle increased, the disruptive level decreased. At an inclination angle of 19°, the inhibition (pathologic signal undetected) occurred at the disturbance level of

2570 µT for 50 Hz and 2640 µT for 60 Hz. On the other hand at 90°, the inhibition began at 1750 µT for 50 Hz and 2020 µT for 60 Hz. We still remark that most of the ICD are non-sensitive to magnetic fields below 1400 µT, where the induced voltage does not exceed the limit of 2 mV according to the standard (EN54505). All the interference threshold curves measured until today have shown that the filter structure or input/output systems used for ICDs have a major influence on their behaviours faced with EMF. The pass band filter structures were found the most sensitive at frequencies between 10 Hz and 100 Hz, and especially at 60 Hz where we can see a lot of interferences. Bipolar electrodes are the most effective remedy for low frequency interferences compared with unipolar electrodes. The present research results substantially improve the currently unsatisfactory situation with regard to the assessment of the safety of persons with active implantable medical devices who are exposed to magnetic fields in the low frequency ranges at their workplace.

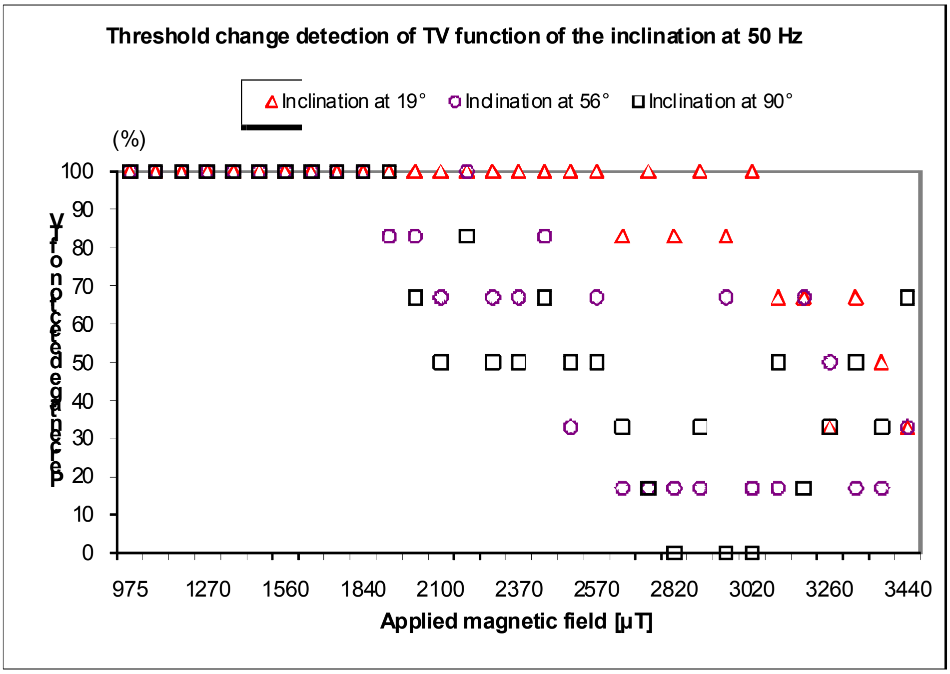

Figure 3. Behaviour of ICD in relation to magnetic field inclination at 50Hz.

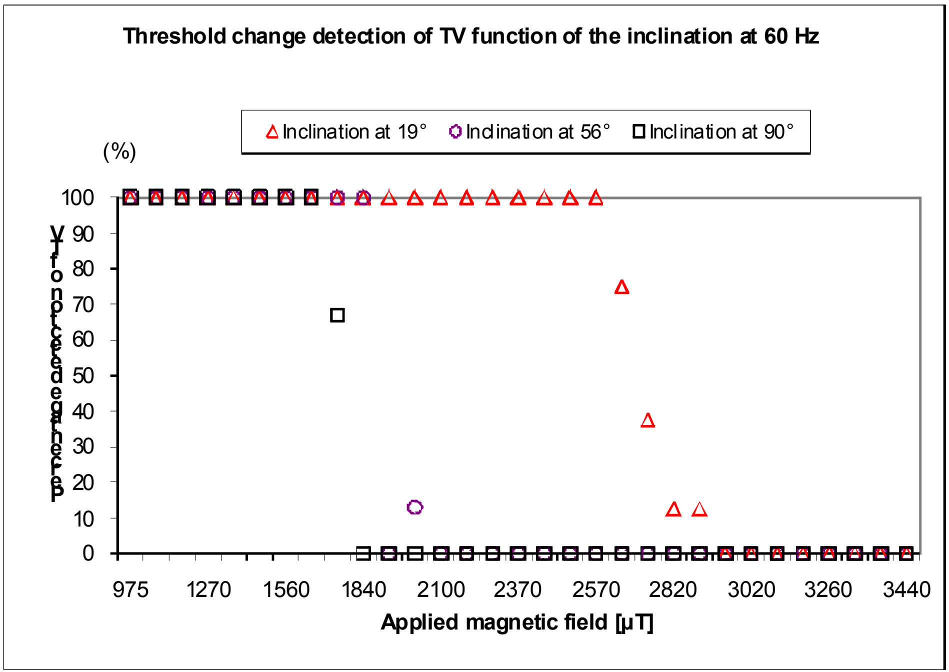

Figure 4. Behaviour of ICD in relation to magnetic field inclination at 60Hz.

Discussion

In this paper we present a protocol and setup dedicated to test the immunity of ICD exposed to low frequency homogenous magnetic fields. We present the methodology used to generate a pathological signal, and we show the influence of the inclination angle on the implant at 50 Hz and 60 Hz. In future work we will test more ICDs at test frequencies up to 100 KHz, and it would be efficient to also test a modulated signal as stated in the standard (EN54505).

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