

# EFFECTS OF EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS ON BIOLOGICAL SYSTEMS

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## ABSTRACT

The effects of Extremely Low Frequency Electromagnetic Fields (3-300kHz) on living beings has been investigated in the last decades since it was demonstrated that there was an increased incidence of childhood leukemia among residences near power lines. Epidemiological and laboratory studies have increased in number since then, however, a definitive cause-effect relationship has not been found yet. The most important reason is a lack of mechanism for the interaction of these non-ionizing, non-thermal electromagnetic fields with biological systems. This overview aims to summarize epidemiological and laboratory *in vivo* and *in vitro* studies made in this field.

**Key Words:** ELF-EMF, Non-ionizing radiation, Signal transduction, Epidemiological

## INTRODUCTION

"...if one used electromagnetic sensors to view the world from space 100 years ago, the world would have looked quite dim. Now, the world glows with electromagnetic (em) energy emissions at most frequencies of the non-ionizing portion of the spectrum. It would be incredible and beyond belief if these electromagnetic fields did

not affect the electrochemical system we call living organisms." This is how Allen Frey poses the problem of the effect low frequency electromagnetic fields on living beings (1).

This striking phrase explains very well the probable consequences of the interaction between very low frequency (VLF) and extremely low frequency (ELF) electromagnetic fields generated from mobile phones, power lines, electrical appliances and such. While mankind has known the effect and the underlying mechanism of high-energy ionizing radiation for a long time the so-called non-ionizing low frequency electromagnetic radiation has been considered to have no impact on living beings.

However, with increasing environmental proximity to high voltage power lines and routine use of household appliances, scientists have become more concerned on the adverse effect of these non-ionizing electromagnetic radiations. In the last 20-30 years a huge amount of epidemiological and laboratory data have accumulated on the interaction of these fields with biological systems indicating a correlation with cancer. The presence of other environmental factors, however, has made it difficult to establish a cause and effect relationship and the overall evidence has been inconsistent and controversial. The studies made in laboratory, both *in vivo* with animal models and

*in vitro* on cell cultures have not been able to clarify these inconsistencies.

The main reason for the controversy concerning EMF exposure and cancer is the lack of a mechanistic explanation that elucidates the impact of EMF with biological systems. Although a number of hypotheses have been put forward (2-4) none have been able to explain the observations made until now.

This review aims to summarize the studies carried out in this field, mainly the so-called extremely low frequency electromagnetic field (ELF-EMF). A brief introduction on the nature of electromagnetic fields is also given for the reader who is unfamiliar with the relevant physical concepts.

### **Electromagnetic fields**

Electromagnetic energy is generated through a change in the state of motion of an electrical charge. The emission or absorption of electromagnetic energy accompanies a change in state of motion. If electrons are caused to move to and fro along a conductor, the conductor acts as a transmitting antenna and emits electromagnetic energy as is in the case of radio waves. When an electric current flows in a wire at extremely low frequency magnetic field forms around and extends out from the wire. An example to this is the power line fields.

Electromagnetic waves, thus generated, have two vectorial components - electric and magnetic field vectors - that vary in space and time and that are perpendicular to each other and to the direction of propagation. The electric field (E) is defined by the force that is exerted on an electrical charge placed in the field and the magnetic (H) field is defined by the force exerted upon a small electric current. E and H vary sinusoidally with a fixed relationship to each other and to time and space. Their unit of frequency of these waves is Hertz (Hz), which is equal to 1 cycle/second.

Electric fields are produced by voltage and increase in strength as the voltage increases. Magnetic fields are produced by flow of currents and increase as the current strength increases. The electric field strength is measured in units of

volts per meter (V/m). Magnetic field, flux densities, are measured in units of gauss (G) or tesla (T) where 10,000 G = 1 Tesla.

Electric fields are shielded by materials that conduct electricity. Even materials that conduct poorly including trees, buildings, and human skin can shield an electrical field. Magnetic fields, on the other hand, pass through most materials and are therefore more difficult to shield. Both fields diminish in strength with distance.

Human exposure to ELF fields is primarily associated with the generation, transmission and use of electrical energy. Electrical energy from generating stations is distributed to communities via high voltage transmission lines, and power lines. Electric and magnetic fields underneath overhead transmission lines may be as high as 12kV/m and 30 $\mu$ T respectively. Electric fields up to 16kV/m and magnetic fields up to 270 $\mu$ T may be found around generating stations and substations. Electric and magnetic fields around most household appliances and equipment typically do not exceed 500V/m and 150 $\mu$ T respectively. However, these values depend on many factors including the distance from power lines, the number and type of these appliances and the electrical wiring of the house. In all cases the field intensities decrease rapidly with distance. The electric and magnetic field intensities in workplaces are much higher and can reach values as high as 50mT near induction furnaces or 25kV/m in generating stations (5).

The electromagnetic energy spectrum Fig.1 encompasses the wavelengths from  $3 \times 10^7$  meters (extremely low frequency) to 0.003 angstroms (gamma rays). Very low frequency (VLF) and extremely low frequency (ELF) electromagnetic fields encompass the frequencies from 3kHz to 30kHz and from 3Hz to 3kHz respectively. With increasing frequencies it is difficult to separate the magnetic from the electric components of the field. However at ELF whether mostly an electric or a magnetic interaction will occur depends on the techniques of field application. As for population exposure the ELF-EMF source characteristics, the distance and the presence of any shielding materials like buildings etc. will determine whether the interaction depends mostly on the electric or magnetic component of the ELF-EMF.

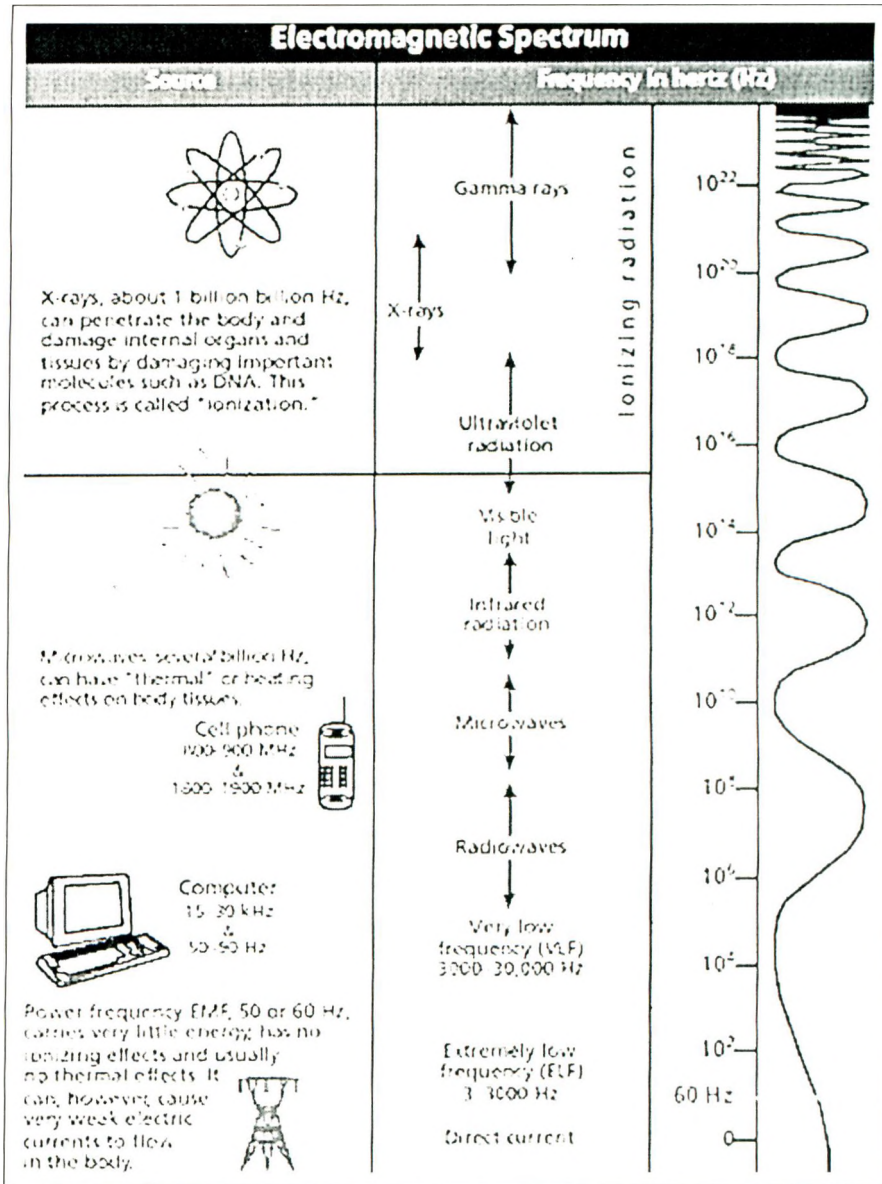


Fig. 1: The electromagnetic spectrum

While for a long time it was known that high frequency radiation (X-rays,  $\gamma$  rays) causes ionization of the macromolecules and thus can be lethal to cells, low frequency and very low frequency radiation was considered to be safe. The reason to this belief was that ELF-EMF did not cause ionization or any appreciable heat effects. However, with the increase of the man made electrical devices and their widespread use, public concern on the possible health effects of these low frequency EMF have increased. The term "Electropollution" is often used to describe the effects of the Non-ionizing Electromagnetic Radiation which is emitted by electrical power

lines, power stations, transformers, electrical appliances, microwave appliances, electrical blankets, steel pipes, reinforcement bars that conduct an electrical current and underground transport systems.

**Electropollution**

Living beings, which are complex electrochemical systems have evolved over million of years in a world with a relatively weak magnetic field and with few electromagnetic energy emitters. They have been exposed to the

natural geomagnetic field equal to about 0.5 gauss depending on latitude and to the geoelectric field, about 100V/m on the earth's surface under fair weather conditions and which can reach several thousand V/m in a thunderstorm. Organisms, including humans, have adapted to this electromagnetic radiation and have been using it to regulate various cellular functions such as the modulation of the circadian rhythms, sensing their prey, and navigation (6).

With the advent of technological developments, man-made electromagnetic sources with a very wide range of frequencies, intensities and modulations have increased enormously since the last decades. Living organisms have, thus, suddenly found themselves in this new environment, which they have not had the opportunity to adapt to. Thus it is unthinkable, as Allen Frey puts it that this sudden change may have no impact on biological systems. Although until now controversial results have been obtained and discussions on whether these fields have serious deleterious effects or not are still going on, enough data have accumulated to indicate that these low frequency electromagnetic fields do interact "somehow" with biological systems.

How can we explain the observations made in the numerous researches? A substance that is foreign to a living organism and that may be toxic affects the living organism in a "dose-response relationship" i.e. a linear relationship where as the dose increases the resultant effect also increases. Theory and data show that this is not correct for the interaction of ELF-EMF with living beings. Rather living beings are electrochemical systems that use low frequency electromagnetic fields in a lot of cellular and physiological functions from nervous system to protein folding. Thus, any interaction between ELF-EMF and a living organism can occur only if the exogenous field comes into a sort of "resonance" with the endogenous field produced by the living being. This explains the so called "window" effect. A "window" effect means that only certain intervals in a spectrum cause an interaction between two phenomena. It is by now accepted that there are specific "window"s of effectiveness for certain carrier and modulation frequencies and intensities although attempts to explain and

determine these "window"s have not been successful as yet (7).

## **Epidemiological Data**

### **Residential Studies**

Scientific evidences suggesting that ELF-EMF exposures may pose health risks are inconsistent. In 1979 Wertheimer and Leeper in their pioneering work reported an association between residential exposures of ELF-EMF and childhood leukemia (8). Since then, a large number of studies have been conducted to assess an association between ELF-EMF exposure and cancer. However, epidemiological studies have serious limitations in their ability to demonstrate cause-effect relationship due to the uncontrolled environmental factors such as socioeconomic factors, air pollution and exposure to chemicals. This has made it difficult to arrive to a consistent conclusion on the adverse effect of electromagnetic fields on human beings.

After the pioneering work of Wertheimer and Leeper, there have been more than a dozen studies on childhood cancer and exposure to low frequency electromagnetic fields. These studies estimated magnetic field exposure from short-term measurements, long term measurements or on the basis of distance between the home and power lines. The results of these studies relating to leukemia are the most consistent. Out of 13 studies all but five reported relative risk estimates of between 1.5 and 3.0 (8-20).

Studies that have examined the use of electrical appliances, primarily electrical blankets, have also resulted in controversial results. A study conducted by Savitz et al. in Denver (21) suggested a link with prenatal use of electric blankets, another carried out in Los Angeles by London et al. (14) found an association between leukemia and children using hair dryers and watching monochrome television. However, the studies of Li et al. (22). Vena et al.(23) and others have reported negative results.

The consistencies of the results on ELF-leukemia correlation studies carried out at locations near power lines, led the U.S.National Academy of Sciences Committee (NAS) to conclude that

children living near power lines are at increased risk of leukemia (24). It was declared that although the confidence intervals are wide the results were consistent with a pooled relative risk of 1.5.

After the NAS committee completed its review, Tynes and Haldorsen reported the results of a study made in Norway in 1997 (20). This study included 500 cases of all types of childhood cancer in individuals who lived nearby transmission lines. No association between leukemia risk, brain cancer or lymphoma and magnetic field was observed. However, the number of exposed cases was small. On the other hand, in a case-control study performed in Germany by Michaelis et al. in 1997 (18), on 129 cases and 328 controls, an elevated relative risk of 3.2 for magnetic field intensities greater than  $0.2\mu\text{T}$  was found.

Linnet et al. carried out a large case-control study on 638 cases and 620 controls in U.S. in 1997 (19). Magnetic field measurements were determined using 24-hour time-weighted average measurements in the bedroom and 30 second measurements in other rooms. The measurement results were found to be suggestive of a positive association between magnetic fields and leukemia risk.

### Occupational Studies

A large number of studies have been carried out to determine possible links between exposure to ELF-EMF and cancer risk among workers in electrical occupations. In the first study made by Milham in 1982 (28), an excess risk for leukemia was found among electrical workers. Savitz and Ahlbom (29) found that the types of cancer for which elevated rates under exposure to ELF were noted, varied in different studies when cancer subtypes were characterized. Increased risks of various types of leukemia and nervous tissue tumors and male or female breast cancer were also reported (30-33). However, these results were both inconsistent and had not taken into account other environmental factors like benzene solvent in the workplace.

Subsequent studies have attempted to overcome some of the deficiencies in the earlier works by measuring ELF field exposure at the workplace and by taking duration of work into consideration.

An elevated cancer risk among exposed individuals was observed, but the type of cancer varied. Although Savitz and Loomis (34) found no association, Floderus et al. (35) found a significant association with leukemia and Thériault et al. (36) also noted a link, but one that was weak and not significant. For nervous tissue tumors Floderus et al. (35) found an excess for glioblastoma (astrocytoma III-IV) while both Thériault et al. (36) and Savitz and Loomis (34) found only suggestive evidence for an increase in glioma (astrocytoma I-II).

Many studies were also made to investigate the possibility that ELF electric fields could be linked to cancer. Thériault et al. (36) analyzed also electric fields and found that workers with leukemia at one of the utilities were more likely to have been exposed to electric fields than control groups. The association was stronger in a group that had been exposed to high electric and magnetic fields (37). At a second utility, no association was found between leukemia and higher cumulative exposure to workplace electric fields but an association was found with brain cancer (26).

As can be seen in this short overview, the results on the epidemiological studies to assess a relationship between cancer and extremely low frequency electromagnetic fields have not yielded a positive correlation. The above-mentioned limitations of epidemiological studies may be the major reason for the controversial results. However, it is apparent that extremely low frequency electromagnetic fields may be associated to childhood cancer. The US National Institute of Environmental Health Sciences (NIEHS) convened an international Working Group to review the research results. NIEHS's international panel concluded, using criteria established by the International Agency for research on cancer (IARC), that ELF fields should be considered as a "possible human carcinogen" which is the weakest of three categories used by IARC to classify potential carcinogens. This classification is based on the strength of scientific evidence, not on the strength of carcinogenicity or risk of cancer from the agent. That is it means that while it cannot be excluded that ELF field exposure causes cancer limited evidence exists. Much more high quality research is needed to resolve this issue.

## Physiological Effects

Exposure to a time-varying electric field can result in perception of the field as a result of the alternating electric charge induced on the body surface. Studies have shown that people can perceive 50/60 Hz electric fields stronger than  $20\text{kVm}^{-1}$  (38,39).

Several groups carried out studies on volunteers to assess probable changes in physiological functions. Small changes in cardiac function occurred in volunteers exposed to 60 Hz electric and magnetic fields ( $9\text{kVm}^{-1}, 20\mu\text{T}$ ). (Cook et al., Graham et al.1994) (40,41). Resting heart rate was slightly, but significantly reduced (3-5 beats per minute) during or immediately after exposure. Interestingly this response was absent on exposure to stronger or weaker fields and reduced if the subject was mentally alert. However, Jauchem in his review (42) on the effect of ELF and radio frequency EMF exposure on the cardiovascular system in humans concluded that hazardous effects on exposure were unlikely for the commonly encountered exposure levels. Sander et al. in 1982 (43) and Ruppe et al. in 1995(44) reported that 50Hz and 2-5mT fields caused no physiological or psychological effects. No changes in blood chemistry, blood cell count, blood gases, lactate levels, E.C.G., E.E.G. or circulating hormone levels were observed (41,43), either.

Many studies have reported that volunteers experienced faint flickering visual sensations, known as magnetic phosphenes, during exposure to ELF magnetic fields above 5mT at 60 mT, which can also be induced by direct application of weak electric currents to the head (45). No effects on visually evoked potentials were detected by Sander et al. (43) using 50Hz, 5mT field or Graham et al. (41) using combined 60Hz electric and magnetic fields up to  $12\text{kV}^{-1}$  and  $30\mu\text{T}$ .

It is known by now that induced electric current can stimulate nerve and muscle tissue directly when a current density exceeds threshold values (46). Below threshold values neuronal excitability can still be affected since endogenous electric fields generated by adjacent nerve cells are below these threshold values. Astumian et.al (47) calculated that an electrical signal in the

extracellular field must be greater than approximately 10-100 mV/m, corresponding to an induced current density of 2-20 mA/m<sup>2</sup>, in order to exceed the level of endogenous physical and biological noise in cellular membranes, which are the sites of interaction with ELF-EMF. It has been shown that several structural and functional properties of membranes may be altered in response to induced ELF at or below 100mV/m (48,49). When endogenous electric fields and currents are exceeded in tissues, physiological effects that increase in severity as the current densities increase are observed (46,50).

## Cellular Effects (*in vivo* and *iv vitro*)

Although from epidemiological studies evidence indicating a correlation between ELF-EMF and cancer accumulated in time, these have been inconsistent and controversial. Studies on animal models and cell cultures have neither been able to establish a cause and effect relationship.

The main reason for the controversy on EMF exposure and its biological effect is a lack of mechanism by which the impact of these fields can be explained. The models suggested so far (2-4) have not posed an unambiguous picture of this interaction; however certain facts are now accepted by all scientists in this field.

This interaction is non-linear i.e. it occurs at certain "window"s of frequency and intensity. The electric field cannot penetrate into the cell since the cell membrane acts as an electrical barrier because of its high endogenous electric field. The normal resting potential =  $10^7$  V/m is orders of magnitude less than ELF field intensities. The interaction must occur at the cell membrane surface, causing some kind of electrochemical perturbation in the properties or functions of the membrane. Taking these facts into consideration, the interaction of ELF-EMF with biological systems must be sought in a non-linear mechanism at the cell membrane. Signal transduction is a non-linear mechanism that could explain the bioeffects observed in cells. As a whole, this model assumes that ELF-EMF could alter the surface charge of the cell membrane, involving only the counter-ion layer, come in a frequency dependent resonance with the membrane channels or glycoproteins and

modulate the activity of receptors for ligands such as growth factors, hormones and ion channels.

Laboratory studies both *in vivo* and *in vitro* have provided evidence that exposure to ELF-EMF induces a wide variety of responses. Most of the studies however have concentrated on cell proliferation, differentiation, apoptosis, gene expression, and signal transduction pathways due to their relevance to cancer. For *in vitro* studies many researchers have used pulsed ELF-EMF (PEMF), i.e. electromagnetic field applied in pulses, and have obtained results different than those obtained by continuous sinusoidal waves.

Numerous studies on the impact of ELF-EMF on proliferation of several cell lines have been reported. Alterations in proliferation were observed in studies that used a variety of exposure conditions (magnetic field strengths from 1000 to 5000  $\mu$ T) and cell lines (51-52); but some of these results could not be reproduced by other laboratories that used the same conditions (53). In a detailed study, Katsir et al. (54) reported increased growth over an exposure range of 50 to 100 Hz and 100 to 700  $\mu$ T. Rosenthal and Obe (55) found that exposure of human peripheral lymphocytes to 50 Hz EMF resulted in an enhancement of proliferation. This result was consistent with the results of Johnson et al. who observed that proliferation of T-cells was affected by EMF that were used clinically for bone healing (56). In contrast Zwingelberg et al. (57) showed that exposure of rats to a 50 Hz, 30 mT magnetic fields had no effect on proliferation of peripheral lymphocytes.

The effect of ELF-EMF on differentiation has also been studied extensively. Human fibroblasts were induced to differentiate into post mitotic cells upon exposure to a 20 Hz EMF at 8 mT (58). Tao and Henderson (59) reported that 60 Hz, 1G EMF exposure to cultured hematopoietic progenitor cells, HL-60, induced differentiation. They showed that the effect of EMF was equivalent to the phorbol ester, TPA, and that the effect of EMF and TPA was additive. Conti et al. (60) reported that after 48 hours of exposure, the number phytohaemagglutinin activated or non-activated lymphocytes increased in S phase. Felaco et al. obtained similar conclusions for the S phase while in G1 and G2 phases there were no differences (61).

Induction of apoptosis was also observed by several laboratories with different cell lines (62,63). On the other hand, a study made by Ruiz Gomez (64) using two different cell lines showed no difference on cell cycle distribution and apoptosis between exposed and control cells. It must be noted, however that the ELF-EMF field intensities and frequencies were different.

ELF-EMF's are not known to cause any chromosomal damage (46,65,66) although they have been shown to cause DNA strand breaks (67). Consequently they are not considered to be initiator of cancer like ionizing radiation but rather as promoters (68). That is, they do not induce genetic mutations that initiate the cancer process but they can promote cancer. It is thought that this can be in two ways; either directly by affecting the function of the cell membrane and thus the signal transduction cascade thus causing alterations in the mechanism of cell growth in already pre-cancerous cells, or indirectly by affecting the immune responses to tumors.

It has been shown that ELF-EMF causes an increase in the activity of ornithine decarboxylase (ODC) a marker, which is related to cell proliferation and tumor promotion and is characteristic of many cancer promoters (69,70). ELF-EMF exposure has been shown to affect the ability of T-lymphocytes to destroy tumor cells. Studies with mouse cytotoxic T-lymphocytes and human lymphoma cells showed a 20% to 25% reduction in lymphocyte killing capacity under some frequency and intensity "window"s of ELF-EMF (71). However, Winters found no significant changes in DNA, RNA or proteins in canine and human peripheral blood lymphocytes exposed to 60 Hz, 0.001-0.01 mT magnetic fields (72). These findings imply the importance of the effective "window"s for the impact of ELF-EMF on biological systems.

Consistent with the above observations, *in vitro* studies have revealed that transcription of some genes that participate in the regulation of cell proliferation are altered in ELF-EMF exposed mammalian cells. Philips et al. (73) and other researchers (74) observed changes in the transcription *c-fos*, *c-myc*, *c-jun* and PKC. Attempts were made to identify the DNA regions that might be responsible for the alteration of *c-myc*, *c-fos* and HSP70 transcription under EMF and certain

sites were found to be necessary for these alterations (75,76). However, experimental results of *in vivo* studies on animal models do not support the hypothesis that ELF-EMF exposure by itself has the ability of promoting cancer progression. Instead when used with other tumor promoters it may act as a strong co-promoter (77-80).

Signal transduction starts at the cell surface and is the basis for the communication of the cell. Calcium, being an important mediator of signal transduction cascade is considered to be a plausible site of field interaction. Altered intracellular  $Ca^{+2}$  metabolism results from various ligand-receptor interactions.  $Ca^{+2}$  as a second messenger activates phospholipase C/protein kinase C (PKC) cascade. Many studies have shown that exposure to ELF-EMF changes  $Ca^{+2}$  flux in the cell. Blackman et al. state that numerous studies have shown that ELF-EMF alters the efflux of  $Ca^{+2}$  from CNN derived samples (81). In another study it was found that  $Ca^{+2}$  influx increased during mitogen activated signal transduction in thymic lymphocytes (82). Changes in calcium flux and consequent immune responses were investigated by many researchers (83). This alteration in calcium flux and the consequent effects in signal transduction have been suggested as the possible mechanism for the effect of ELF-EMF on tumor promotion. Theoretical explanations on the interaction of ELF-EMF with calcium ion have been developed by Liboff (2), Blanchard (84) and Lednev (85).

Recent studies that investigated the role of ELF-EMF on PKC signal cascade in B-cell leukemogenesis (the major form of childhood leukemia) showed that *in vitro* exposure to 100 $\mu$ T affected this pathway (86,87). However, these results could not be reproduced in another study (88). Monti et.al (89) detected an elevated level of PKC activity in HL-60 cells exposed to ELF-EMF. Other studies indicated that ELF-EMF could use  $Ca^{+2}$  phospholipid-dependent PKC induction in a way similar to that of TPA or other mitogens (83,90). A very detailed review on the effect of ELF-EMF is done by Tuncel H. (91).

In the last years, researches have been carried out on the effect of ELF-EMF on heat-shock proteins that are known to respond to stress factors and are important in the control of stress in the cell. It has been reported that an increase

was observed in these proteins under field exposure (92,93).

Protein tyrosine kinases, which are important in cell signaling, have also been investigated to determine whether ELF-EMF exposure affects their function. Uçkun et al. found that *Src* protooncogene family PTK LyN as well as its downstream substrate SyK was activated in B-lineage lymphoid cells exposed to a low energy electromagnetic field (60 Hz, 1 G) (87). Subsequent investigations with DT40 lymphoma B- cells showed that in addition to LyN and SyK, the Bruton's tyrosine kinase (BTK) was also stimulated by ELF-EMF exposure (86,94). Lindstrom et al. (95) found that CD45 phosphatase that regulates tyrosine kinase activity of p56lck (a *Src* kinase) was prerequisite for EMF induced oscillations of free intracellular Calcium. This was consistent with the results of Lindstrom, which demonstrated that EMF exposure activated p56lck in Jurkat cells (96).

A number of studies were done on the effect of ELF-EMF on lipid signaling system. Clejan et al. (97) found that exposure to EMF decreased erythropoietin-stimulated phosphatidylinositol 3-kinase activity to lower than basal levels and that phosphatidylinositol specific phospholipase C was activated in TF1 cells. In another investigation, up-regulation of phospholipase D (PC-PLD) was observed (98). These results were consistent with the hypothesis that (86,93) PTKs may be involved in the lipid signal transduction elicited by ELF-EMF.

### Electromagnetic Fields and Bone Healing

The role of ELF-EMF in accelerating bone healing is an outstanding example of its therapeutic application (99). Electrical and electromagnetic stimulation is believed to enhance bone repair, although the effectiveness of these fields depend on their physical characteristics. Low frequency fields have been shown to decrease bone loss and maintain bone mass by decreasing osteoclastic bone removal. Studies on the effects of these fields upon osteoclasts *in vitro* show a decrease in both osteoclastic differentiation and lysosomal enzyme content (100).



**Table 1:** Summary of the ICNIRP exposure guidelines European power

Frequency	European power frequency		Mobile phone base station frequency		Microwave oven frequency
	50 Hz	50 Hz	900 MHz	1.8 GHz	2.45 GHz
	Electric field (V/m)	Magnetic field ( $\mu$ T)	Power density ( $W/m^2$ )	Power density ( $W/m^2$ )	Power density ( $W/m^2$ )
<b>Public exposure limits</b>	5000	100	4.5	9	10
<b>Occupational exposure limits</b>	10000	500	22.5	45	

Interestingly, experiments demonstrate that pulsed low frequency fields are much more effective in stimulating bone healing than high frequency fields (101). Although it has been clinically confirmed that pulsed electromagnetic fields stimulate healing of non-united fractures, their mechanism of action has not been understood.

## Appendix

In 1996, World Health Organization established the International EMF Project to assess the scientific evidence on possible health effects of EMF in the frequency range 0 - 300 GHz. This project that will provide sufficient results to allow more definitive health risk assessment is scheduled to be completed in 2007.

However, based on our present knowledge, standards are set to limit overexposure to electromagnetic field levels present in our environment. Although countries set their own national standards for exposure to electromagnetic fields, the majority of these national standards draw on the guidelines set by the International Commission on Non-ionizing Radiation Protection (ICNIRP). This non-governmental organization, formally recognized by WHO, evaluates scientific results from all over the world. Based on an in-depth review of the literature, ICNIRP produces guidelines recommending limits on exposure. These guidelines are reviewed periodically and updated if necessary.

Electromagnetic field levels vary with frequency in a complex way. Listing every value in every standard and at every frequency would be difficult to understand. The table below is a summary of the exposure guidelines for the three

areas that have become the focus of public concern: electricity in the home, mobile phone base stations and microwave ovens. These guidelines were last updated in April 1998 by ICNIRP (103).

## REFERENCES

1. Frey AH. *Electromagnetic field interactions with biological systems*. *FASEB J* 1992; 7:272-281.
2. Liboff AR. *Geomagnetic cyclotron resonance in living cells*. *J Cell Biol Phys* 1985;13:99-102.
3. Lawrence AF, Adey RA. *Non-linear wave mechanics in interactions between excitable tissue and electromagnetic fields*. *Neurol Res* 1982;4:115-153.
4. Chiabrera A, Viviani R, Caratozzolo F, Giannetti G, Grattarola M, Viviani R. *Electric and magnetic field effects on ligand binding to the cell membrane*. In: Chiabrera A, Nicolini C, Schwan HP, eds. *Interactions between electromagnetic fields and cells*. New York: Plenum Press, 1985:253-281.
5. Bennet WR Jr. *Sources of low-frequency fields*. In: Bennet WR ed. *Health and low-frequency electromagnetic fields*. Michigan USA: Yale Univ, 1994:32-93.
6. Azanza MJ, Del Moral A. *Cell membrane biochemistry and neurobiological approach to biomagnetism*. *Progr Neurobiol* 1994; 44:517-601
7. Adey WR. *Tissue interactions with non-ionizing electromagnetic fields*. *Physiol Rev* 1981;61:435-513.
8. Wertheimer N, Leeper E. *Electrical wiring configurations and childhood cancer*. *Am J Epidemiol* 1979;109:273-84.
9. Fulton JP, Cobb S, Preble E, Leone L, Forman E. *Electrical wiring configurations and*

- childhood leukemia in Rhode Island. *Am J Epidemiol* 1980;111:292-295.
10. Myers A, Cartwright RA, Bonnell JA, Male JC, Cartwright JC. Overhead power lines and childhood cancer. *International Conference of Electric and Magnetic Fields in Medicine and Biology*. London: December 4-5, 1985. IEE Conf. Publ. No. 257. 1985
  11. Tomenius I. 50Hz electromagnetic environment and the incidence of childhood tumors in Stockholm county. *Bioelectromagnetics* 1986;7:191-207.
  12. Savitz DA, Wachtel H, Barnes FA, John EM, Tvrdik JG. Case-control study of childhood cancer and exposure to 60Hz magnetic fields. *Am J Epidemiol* 1988;128:21-38.
  13. Coleman MP, Bell CMJ, Taylor HL, Primic-Zakelj M. Leukemia and residence near electricity transmission equipment: a case-control study. *Br J Cancer* 1989;60:793-798.
  14. London SJ, Thomas DC, Bowman JD, Sobel E, Cheng TC, Peters JM. Exposure to residential electric and magnetic fields and risk of childhood leukemia. *Am J Epidemiol* 1991;134:923-937.
  15. Feychting M, Ahlbom A. Magnetic fields and cancer in children residing near Swedish high voltage power lines. *Am J Epidemiol* 1993;138:467-481.
  16. Olsen JH, Nielsen A, Schulgen G. Residence near high voltage facilities and the risk of cancer in children. *Danish Cancer Registry* 1993;AG-NIR-26
  17. Verkasalo PK, Pukkala E, Hongisto My, et al. Risk of cancer in Finnish children living close to power lines. *Br Med J* 1993;307:895-899.
  18. Michaelis J, Schuz J, Meinert R, et al. Childhood leukemia and electromagnetic fields: results of a population-based case-control study in Germany. *Cancer Causes and Control* 1997;8:167-174.
  19. Linet MS, Hatch EE, Kleinerman RA, et al. Residential exposure to magnetic fields and acute lymphoblastic leukemia in children. *New Engl J Med* 1997;333:1-7.
  20. Tynes T, Haldorsen T. Electromagnetic fields and cancer in children residing near Norwegian high voltage power lines. *Am J Epidemiol* 1997;145:219-226.
  21. Savitz DA, John EM, Kleckner RC. Magnetic field exposure from electric appliances and childhood cancer. *Am J Epidemiol* 1990;131:763-773.
  22. Li D, Ceckoway H, Mueller BA. Electric blanket use during pregnancy in relation to the risk of congenital urinary tract anomalies among woman with a history of subfertility. *Epidemiology* 1995;6:485-489.
  23. Vena JE, Graham S, Hellman R, Swanson M, Brasure J. Use of electric blankets and risk of post-menopausal breast cancer. *Am J Epidemiol* 1991;134:180-185.
  24. National Academy of Sciences Committee. *Possible Health Effects of Exposure to Residential Electric and Magnetic Fields*. The National Academy Press 1997.
  25. United Kingdom cancer Study Investigators. Exposure to power frequency magnetic fields and the risk of childhood cancer: a case-control study. *Lancet* 1999;354:1925-1931.
  26. Guénel P, Nicolau J, Imbernon E, Chevalier A, Goldberg M. Exposure to 50Hz electric field and incidence of leukemia, brain tumor, and other cancers among French electric utility workers. *Am J Epidemiol* 1996;144:1107-11021.
  27. Preston-Martin S, Navidi W, Thomas D, Lee PJ, Bowman J, Progoda J. Los Angeles study of residential magnetic fields and childhood brain tumors. *Am J Epidemiol* 1996;143:105-119.
  28. Milham S Jr. Mortality from leukemia in workers exposed to electric and magnetic fields. *New Engl J Med* 1982;307:249.
  29. Savitz DA, Ahlbom A. Epidemiologic evidence on cancer in relation to residential and occupational exposure. In: *Biologic effects of electric and magnetic fields*. Vol. 2. New York: Academic Press, 1994:233-262.
  30. Demers PA, Thomas DB, Strenhagen A, et al. Occupational exposure to electromagnetic fields and breast cancer in men. *Am J Epidemiol* 1991;132:775-776.
  31. Matanoski GM, Breyse PN, Elliott EA. Electromagnetic field exposure and male breast cancer. *Lancet* 1991;337:773.
  32. Tynes T, Andersen A, Langmark F. Incidence of cancer in Norwegian workers potentially exposed to electromagnetic fields. *Am J Epidemiol* 1992;136:81-88.
  33. Loomis DP, Savitz DA, Ananth CV. breast cancer mortality among female electrical workers in the United States. *J Nat Cancer Inst* 1994;86:921-925.
  34. Savitz DA, Loomis DP. Magnetic field exposure in relation to leukemia and breast cancer mortality among electrical utility workers. *Am J Epidemiol* 1995;141:123-134.

35. Floderus B, Persson T, Stenlund C, Wennberg A, Ost A, Knave B. Occupational exposure to electromagnetic fields in relation to leukemia and brain tumors: a case-control study in Sweden. *Cancer Causes and Control* 1993;4:465-476.
36. Thériault S, Goldberg M, Miller AB, et al. Cancer risks associated with occupational exposure to magnetic fields among electric utility workers in Ontario and Quebec, Canada and France -1970-1989. *Am J Epidemiol* 1994;139:550-572.
37. Miller AB, To T, Agnew DA, Wall C, Green LM. Leukemia following occupational exposure to 60Hz electric and magnetic fields among Ontario electric utility workers. *Am J Epidemiol* 1996;144:150-160.
38. United Nations Environmental Programme/ World Health Organization/ International Radiation Protection Association. Extremely low frequency (ELF) fields. Geneva, World Health Organization. *Environmental Health Criteria* 1984;35.
39. Tenforde TS. Biological interactions of extremely low frequency electric and magnetic fields. *Bioelectrochem Bioenerg* 1991;25:1-17.
40. Cook MR, Graham C, Cohen HD, Gerkovich MM. A replication study of human exposure to 60-Hz field effects on neurobehavioral measures. *Bioelectromagnetics* 1992;13:261-285.
41. Graham C, Cook MR, Cohen HD, Gerkovich MM. Dose response study of human exposure to 60-Hz electric and magnetic fields. *Bioelectromagnetics* 1994;15:447-463.
42. Jauchem RJ. Exposure to extremely-low-frequency electromagnetic fields and radiofrequency radiation: cardiovascular effects in humans. *Int Arch Occup Environ Health* 1997;70:9-21.
43. Sander R, Brinkmann J, Kühne B. Laboratory studies on animals and human beings exposed to 50-Hz electric and magnetic fields. CIGRE, international Congress on Large High Voltage Electric Systems, Paris, 1-9 Sept. 1982, CIGRE Paper:36-01.
44. Ruppe I, Hentschel K, Eggert S, Goltz S. Experimentelle Untersuchungen zur Wirkung von 50 Hz magnetfeldern. *Schriftenreihe der Bundesanstalt für Arbeitmedizin* 1995;11.003.
45. Silny J. The influence threshold of a time-varying magnetic field in the human organism. In: Bernhardt JH, ed. *Biological effects of static and extremely-low frequency magnetic fields*. Munich, MMV Medizin Verlag 1986;105-112.
46. Tenforde TS. Interaction of ELF magnetic fields with living systems. In: Polk C, Postow E, eds. *Biological effects of electromagnetic fields*. Boca Raton: FL, CRC Press, 1996:185-230.
47. Astumian RD, Weaver JC, Adair RK. Rectification and signal averaging of weak electric fields by biological cells. *PNAS* 1995; 92:3740-3743.
48. Tenforde TS. Cellular and Molecular pathways of extremely low frequency electromagnetic field interactions with living systems. In: Blank M, ed. *Electricity and magnetism in biology and medicine*. San Fransisco: San Fransisco Press, 1993:1-8.
49. Sienkiewicz ZJ, Saunders RD, Kowalczyk Ci. The biological effects of exposure to non-ionizing electromagnetic fields and radiation: Extremely low frequency electric and magnetic fields. Chilton, UK: National Radiological Protection Board, 1991, NRPB R239.
50. Bernhardt JH. The direct influence of electromagnetic fields on nerve and muscle cells of man within the frequency range of 1 Hz to 30 MHz. *Radiat Environ Biophys* 1979;16:309-323.
51. Antonopoulos A, Yang B, Stamm A, Heller WD, Obe G. Cytological effects of 50 Hz electromagnetic fields on human lymphocytes in vitro. *Mutation Res* 1995; 346:151-157.
52. West RW, Hinson WG, Lyle DB, Swicord ML. Enhancement of anchorage-independent growth in JB6 cells exposed to 60 Hz magnetic fields. *Bioelectrochem Bioenerg* 1994;34:39-43.
53. Snawder JE, Edwards RM, Conover DL, Lotz WG. Effect of magnetic field exposure on anchorage-independent growth of a promoter sensitive mouse epidermal cell line (JB6). *Environ Health Perspect* 1999;107:195-198.
54. Katsir G, Baram S, Parola A. Effect of sinusoidally varying magnetic fields on cell proliferation and adenosine deaminase specific activity. *Bioelectromagnetics* 1998; 19:46-52.
55. Rosenthal M, Obe G. Effects of 50 Hz electromagnetic fields on proliferation and on chromosomal alterations in human

- peripheral lymphocytes untreated or pretreated with chemical mutagens. *Mutation Research* 1989;210:329-335.
56. Johnson MT, Vanscoy-Cornett A, Vesper DN, Swez JA, Chamberlain JK, Seaward MB, Nindi G. Electromagnetic fields used clinically to improve bone healing also impact lymphocyte proliferation in vitro. *Biomed Sci Instrum* 2001;37:215-220.
  57. Zwingelberg R, Obe G, Rosenthal M, Mevissen M, Buntenkotter S, Loscher W. Exposure of rats to a 50 Hz, 30 mT magnetic field influences neither the frequencies of sister-chromatid exchanges nor proliferation characteristics of cultured peripheral lymphocytes. *Mutation Res* 1993;302:39-44.
  58. Rodemann HP, Bayreuther K, Pfeleiderer G. The differentiation of normal and transformed human fibroblasts in vitro is influenced by electromagnetic fields. *Exp Cell Res* 1989;182:610-621.
  59. Tao Q, Henderson A. EMF induces differentiation in HL-60 cells. *J Cellular Biochem* 1999;73:212-217.
  60. Conti P, Reale M, Grilli A, Barbacane RC, Di Luzio S, Di Gioacchino M, De Lutiis MA, Felaco M. Effect of electromagnetic fields on several CD markers and transcription and expression of CD. *Immunobiology* 1999;201:36-48.
  61. Felaco M, Reale M, Grilli A, De Lutiis MA, Barbacane RC, Di Luzio S, Conti P. impact of extremely low frequency electromagnetic fields on CD4 expression in peripheral blood mononuclear cells. *Mol Cell Biochem* 1999; 210:49-55.
  62. Flipo D, Fournier M, Benquet C, Roux P, Le Boulaire C, Pinsky C, La Bella FS, Krzystyniak K. increased apoptosis, changes in intracellular Ca<sup>2+</sup>, and functional alterations in lymphocytes and macrophages after in vitro exposure to static magnetic field. *J Toxicol Environ Health A* 1998; 54:63-76.
  63. Shoji M, Girard PR, Mazzei GJ, Vogler WR, Kuo JF. immunocytochemical evidence for phorbol-ester induced protein kinase C translocation in HL-60 cells. *Biochem Biophys Res Comm* 1986;135:1143-1149.
  64. Ruiz Gomez MJ, De la Pena L, Pastor JM, Martinez Morillo M, Gill L. 25Hz electromagnetic field exposure has no effect on cell cycle distribution and apoptosis in U-937 and HCA-2/1cch cells. *Bioelectrochemistry* 2001;53:137-140.
  65. Scarfi MR, Lioi MB, Zeni O, Franceschetti G, Franceschi C, Bersani F. Lack of chromosomal aberration and micronucleus induction in human lymphocytes exposed to pulsed magnetic fields. *Mutation Res.* 1994;306:129-133.
  66. Paile W, Jokela K, Koivistoinen A, Salomaa S. Effects of 50 Hz sinusoidal magnetic fields and spark discharges on human lymphocytes in vitro. *Bioelectrochem Bioenerg* 1995;36:15-22.
  67. Sarkar S, Sher A, Behari J. Effect of low power microwave on the mouse genome: a direct DNA analysis. *Mutation Research* 1994;320:141-147.
  68. Adey WR. ELF magnetic fields and promotion of cancer: experimental studies. in: Norden B, Ramel C, eds. interaction of low-level electromagnetic fields in living systems. New York: Oxford University Press. 1992:23-47.
  69. Litovitz TA, Krause D, Mullins JM. Effect of coherence time of the applied magnetic field on ornithine decarboxylase activity. *Biochem Biophys Res Comm* 1991; 178:862-865.
  70. Byus CV, Pieper SE, Adey WR. The effects of low-energy 60 Hz environmental electromagnetic fields upon the growth-related enzyme ornithine decarboxylase. *Carcinogenesis* 1987;8:1385-1389.
  71. Lyle DB, Ayotte RD, Sheppard AR, Adey WR. Suppression of T lymphocyte cytotoxicity following exposure to 60 Hz sinusoidal electric fields. *Bioelectromagnetics* 1988; 9:303-313.
  72. Winters WD, Wendell D. Biological functions of immunologically reactive human and canine cells influenced by in vitro exposure to 60 Hz electric and magnetic fields. Final report, New York State Power Lines Project, Contract no. 218207. Sept. 25, 1986, Wadsworth Center for Laboratories and Research, Albany NY 12201.
  73. Philips JL, Haggren W, Thomas WJ, Ishida-Jones T, Adey WR. Magnetic field induced changes in specific gene transcription. *Biochem Biophys Acta* 1992;1132:140-144.
  74. Lagroy I, Poncy JL. Influences of 50 Hz magnetic fields and ionizing radiation on c-jun and c-fos oncoproteins. *Bioelectromagnetics* 1998;19:112-116
  75. Rao S, Henderson AS. Regulation of c-fos is affected by electromagnetic fields. *J Cellular Biochem* 1996;63:358-365.

76. Lin H, Blank M, Rossol-Haseroth K, Goodman R. Regulating genes with electromagnetic response elements. *J Cell Biochem* 2001; 81:143-148.
77. McLean JR, Stuchly MA, Mitchel RE, et al. Cancer promotion in mouse-skin model by a 60 Hz magnetic field. Tumor development and immune response. *Bioelectromagnetics* 1991;12:273-287.
78. Rannung A, Ekstrom T, Mild KH, Holmberg B, Gimenez-conti I, Slaga TJ. A study on skin tumor formation in mice with 50 Hz magnetic field exposure. *Carcinogenesis* 1993;14:573-578.
79. Repacholi MH, Basten A, Gebiski V, Noonan D, Finnie J, Harris AW. Lymphomas in E mu-Pim1 transgenic mice exposed to pulsed 900 MHz electromagnetic fields. *Radiat Res* 1997;147:631-640.
80. Cain CD, Thomas DL, Adey WR. 60 Hz magnetic field acts as co-promoter in focus formation of C3H/10T1/2 cells. *Carcinogenesis* 1993;14:955-960.
81. Blackman CF, Benane SG, Elliott DJ. Influence of electromagnetic fields on the efflux of calcium ions from brain tissue in vitro: A three model analysis consistent with the frequency response up to 510 Hz. *Bioelectromagnetics* 1988;9:215-227.
82. Liburdy RP. Calcium signalling in lymphocytes and ELF fields: Evidence for an electric field metric and a site of interaction involving calcium ion channel. *FEBS Lett* 1992;301:53-59.
83. Wallaczek J. Electromagnetic field effects on cells of the immune system: the role of calcium signalling. *FASEB J* 1992; 6:3176-3185
84. Blanchard PJ, Blackman CF. A model of magnetic field effects on biological systems with confirming data from a cell culture preparation. In: Frey A, ed. *On the nature of electromagnetic field interactions with biological systems*. Medical Intelligence Unit. Maryland, USA: Springer, 1995:43-58.
85. Lednev VV. Interference with the vibrational energy sublevels of ions bound in calcium-binding proteins as the basis for the interaction of weak magnetic fields with biological systems. In: Frey A, ed. *On the nature of electromagnetic field interactions with biological systems*. Medical Intelligence Unit. Maryland, USA: Springer 1995:59-73.
86. Dibirdik I, Kristupaitis D, Kurosaki T, et al. Stimulation of Src family protein-tyrosine kinase as a proximal and mandatory step for Syk kinase-dependent phospholipase C( $\gamma$ )2 activation in lymphoma B-cells exposed to low energy electromagnetic fields. *J Biol Chem* 1998;273:4035-39.
87. Uckun FM, Kurosaki T, Jin J, et al. Exposure of B-lineage lymphoid cells to low energy electromagnetic fields stimulates lyn kinase. *J Biol Chem* 1995;270:27666-27670
88. Miller SC, Furniss MJ. Bruton's tyrosine kinase activity and inositol-1,4,5-triphosphate production are not altered in the DT40 lymphoma B cells exposed to power line frequency magnetic fields. *J Biol Chem* 1998;273:32618-32626.
89. Monti MG, Pernecco L, Morussi MS, Battini R, Zaniol P, Barbiroli P. Effects of ELF pulse electromagnetic fields on protein kinase C activation process in HL-60 leukemia cells. *J Bioelectricity* 1991;10:119-131
90. Goodman R, Chizmandzhev y, Henderson AS. Electromagnetic fields and cells. *J Cell Biochem* 1993;51:436-441.
91. Tuncel H. Effects of electromagnetic fields on the immune system. In: P. Stravroulakis ed. *Biological effects of electromagnetic fields*. Heidelberg: Springer-Verlag, 2003: 494-503.
92. Lin H, Opler M, Head M, Blank M, Goodman R. Electromagnetic field exposure induces rapid, transitory heat shock factor activation in human cells. *J Cell Biochemistry* 1995; 66:482-488.
93. Lin H, Head M, Blank M, Han L, Jin Mi Goodman R. Myc-mediated transactivation of HSP70 expression following exposure to magnetic fields. *J Cell Biochemistry* 1998; 69:181-188.
94. Kristupaitis D, Dibirdik I, Vassilev A, Mahajan S, Kurosaki T, Chu A, Tuel-Ahlgren L, Tuong D, Pond D, Luben R, Uckun FM. Electromagnetic field induced stimulation of Bruton's tyrosine kinase. *J Biol Chem* 1998; 273:12397-12401
95. Lindstrom E, Berglund A, Mild KH, Lindstrom P, Lundgren E. CD45 phosphatase in Jurkat cells is necessary for response to applied ELF magnetic fields. *FEBS Lett* 1995; 370:118-122.
96. Lindstrom E, Still M, Mattsson MO, Mild KH, Luben RA. ELF magnetic fields initiate protein tyrosine phosphorylation of the T cell receptor complex. *Bioelectrochemistry* 2001;53:73-78.

97. Clejan S, Dotson RS, Ide CF, Beckman BS. Coordinated effects of electromagnetic field exposure on erythropoietin-induced activities of phosphatidylinositol-phospholipase C and phosphatidylinositol 3-kinase. *Cell Biochem Biophys* 1995; 27:203-225.
98. Clejan S, Ide C, Walker C, Wolf E, Corb M, Beckman B. Electromagnetic field induced changes in lipid second messengers. *J Lipid Mediat Cell Signal* 1996;13:301-324.
99. Einhorn TA. Enhancement of fracture-healing. *J Bone Joint Surg. (American Volume)* 1995;77:940-956.
100. Behari J. Electrostatic stimulation and bone fracture healing. *Critical Rev in Biomed Eng* 1991;18:235-254.
101. Otter MW, Qin YX, Rubin CT. Effects of electromagnetic fields in experimental fracture repair. *Clin Orthop Relat R* 1998; 365:90-104.
102. ICNIRP. EMF Guidelines. *Health Physics* 1998;74:494-522.